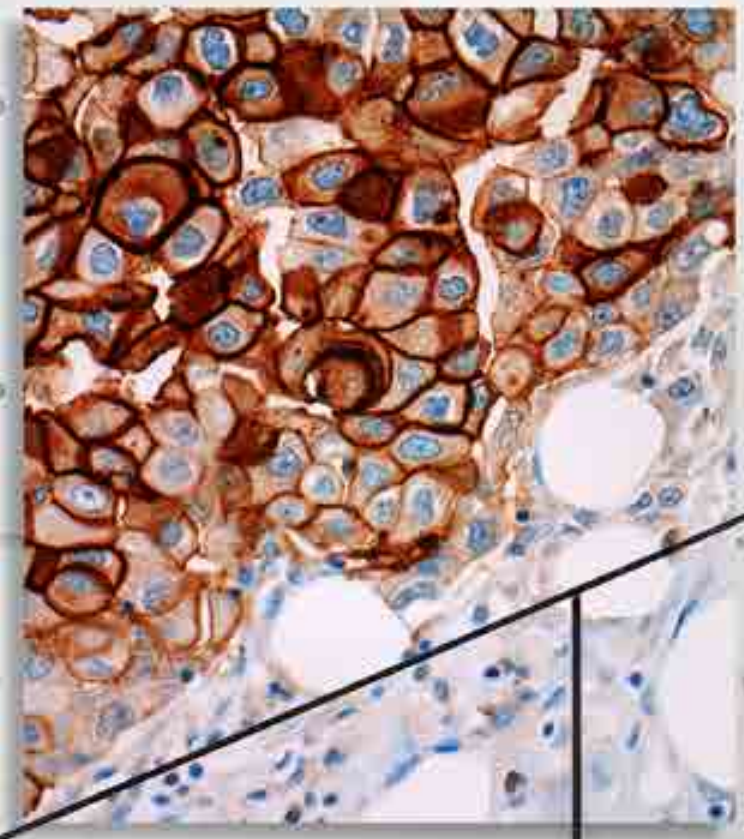
Centre for Cancer Biomarkers

Norwegian Centre of Excellence – University of Bergen

Norwegian Centre of Excellence

The Research Council of Norway



Annual Report 2018

Annual Report 2018

Highlights

8-17
CCBIO OPINIONS

22-27
SCIENTIFIC ACTIVITIES

29-55
RESEARCH TEAMS

56-61
INTERNATIONAL FACULTY

62-67
RESEARCH SCHOOL

113-120
PUBLICATIONS

TABLE OF CONTENTS

EDITORS: Lars A. Akslen, Eli Synnøve Vidhammer, Geir Olav Løken
COVER PICTURE: Ingvild Festervoll Melien
PHOTOGRAPHERS: Ingvild Festervoll Melien, Eli Synnøve Vidhammer, Geir Olav Løken, Elisabeth Wik, Anne Sidsel Herdlevær, Jørgen Barth, Lars A. Akslen, Ingeborg Winge, Kenneth Finne, Kim Andreassen, Emmet McCormack, Bjørn Tore Gjertsen, Dana Costea, Camilla Krakstad, Pugazendhi Murugan Erusappan, John Cairns, AMC Gillissen, Colourbox, Yves Aubert
ILLUSTRATIONS: Gautehatlem.no, Shutterstock
ART DIRECTION / LAYOUT: Gautehatlem.no

Director's comments

There are many roads to Rome, - and Rome was not built in one day. Likewise, there are many mechanisms promoting excellence in science. The definition of excellence is multi-dimensional, with both personal and institutional criteria, and not easy to agree on. At the same time, the metrics of excellence are evasive. On an individual level, elements such as novelty, creativity, quality over quantity, ambition, vision, perspective, well-organized teams and partnerships, and research integrity, among others, are needed. As indicated by Bruce Zetter, "You have to compete with yourself and exceed the ordinary standards." Certainly true but correspondingly difficult.

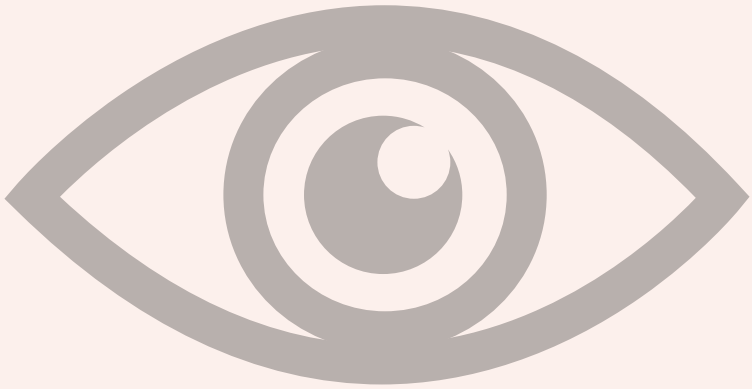
Multiple projects have been initiated and developed during CCBIO's first 5-year period, on various solid and liquid cancers, using biomarker profiling of solid tissues and liquid samples for discovery and validation. During the second term, increased focus will be put on protein mapping and deep tissue profiling. CCBIO recently established equipment for imaging mass cytometry as the first laboratory in Scandinavia, and this move has been received with enthusiasm by our teams. It is well recognized that spatial resolution is needed to increase the precision and sensitivity of molecular tissue mapping. The issue is "location, location, location."

CCBIO as a research orchestra is constantly changing. Supporting the ongoing projects, a range of educational and training activities have been established. During 2018, Associate Investigator Elisabeth Wik was appointed as the new coordinator of the CCBIO Research School for Cancer Studies and immediately put her fingerprint on many initiatives. Notably, the INTPART-supported 3-week course in cancer-related vascular biology was arranged together with our partners from the Vascular Biology Program (VBP) at Boston Children's Hospital and Harvard Medical School, directed by Marsha A. Moses. The interactive teaching in lectures and during discussion of assignments was a true inspiration, and we are very grateful to the VBP faculty for their support. The first cycle of student exchange between Bergen and Boston was completed during the summer of 2018.

As usual, several CCBIO "opinions" have been included in this annual report. The challenge of data overload is commented on by Strand & Jonassen. They quote the philosopher Karl Popper warning that "too many dollars may chase too few ideas" and that "big science may destroy great science, and the publication explosion may kill ideas." Gullberg & Östman reflect on the dualism of the cancer stroma and cancer associated fibroblasts, which might have both stimulatory and inhibitory properties depending on tissues and biological context. In a piece by Bourdon & Gjertsen, a new wave of p53 biology is discussed, stimulated by the appearance of p53 isoforms and their roles in cancer progression. CCBIO PhD candidate Engen reflects on the outcome of novel targeted cancer therapies and the importance of a balanced view on the true benefits. In the final contribution by Aubert, the importance of innovation for real life impact is underscored.

The steps in the stairways to excellence need to be recognized and reflected on, and CCBIO will continue to support its many driving mechanisms. Whereas novel ideas is the real fundament, this must be combined with methodological developments involving new technology and strategies for big data processing. In the years to come, deep tissue profiling and molecular mapping of intact tissues will be an important area of interest. ••

Lars A. Akslen, Director of CCBIO



Vision and Research Areas

CCBIO aims to discover, validate and translate functional cancer biomarkers to improve our understanding of tumor mechanisms, promote early diagnosis of aggressive phenotypes, and support 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 (Basic Studies)

2. Exploration and Validation of Cancer Biomarkers (Biomarker Validation)

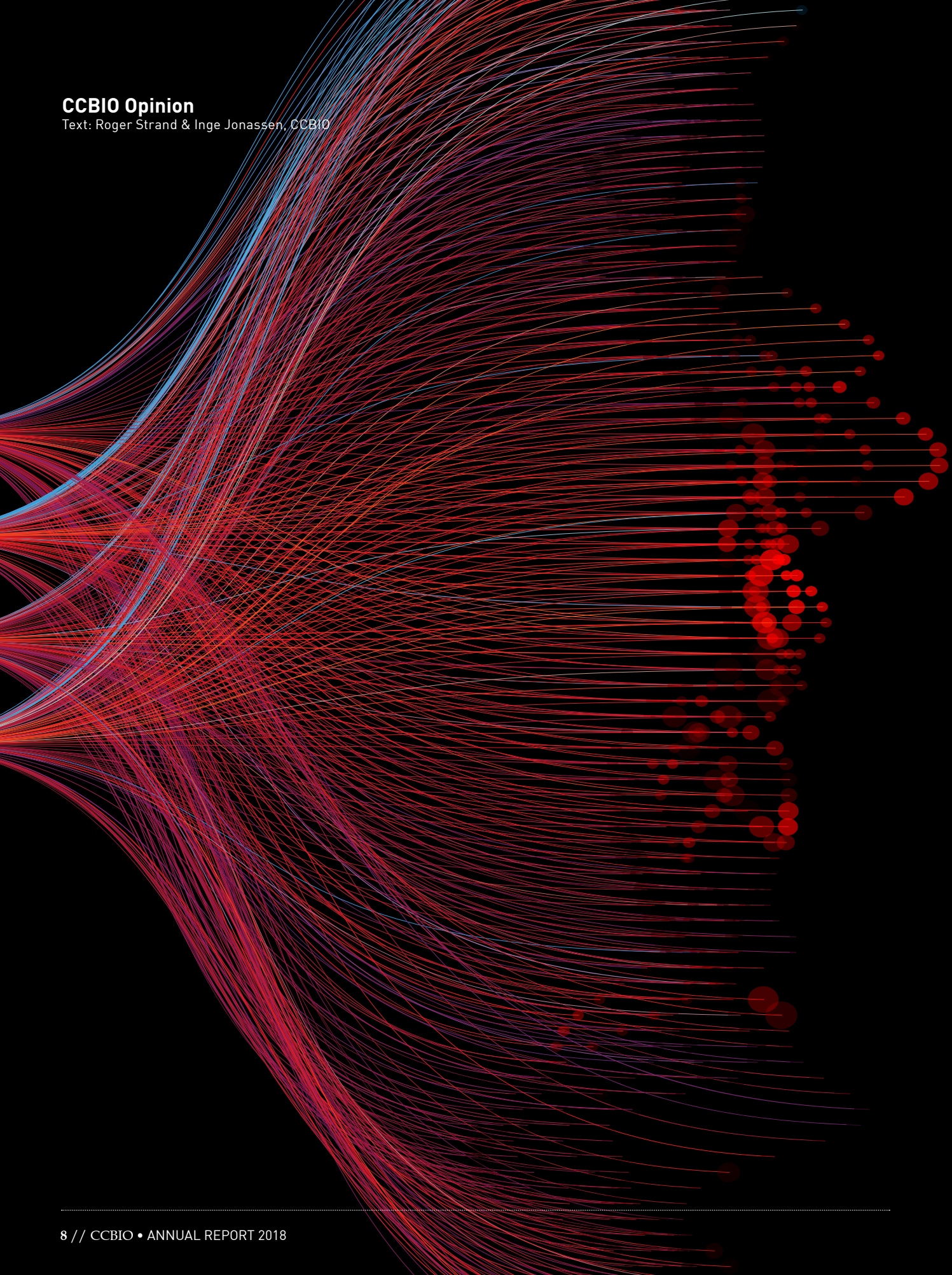
3. Clinical Applications and Trial Studies (Clinical Studies)

4. Ethics, Economics and Priorities (Societal 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 these programs. ••

CCBIO Opinion

Text: Roger Strand & Inge Jonassen, CCBIO



Too Much Data? The Gastro Perspective

In popular culture, "TMI" denotes "Too Much Information". You ask someone "How are you today?" and he replies "Good, much better than last week when I was so constipated. This morning I was quite flatulent but it seems to have passed." In almost any other context than that of gastroenterology, this is Too Much Information. A simple "I'm fine, thank you" would do well.

In contemporary science, the equivalent of constipation and flatulence is caused by the uncontained acquisition of Too Much Data. A Nature editorial (2016) reported a future estimate of 0.4 terabytes (TB) of clinical data, 6 TB of genomics data and 1,100 TB "additional data" per patient. 1,100 TB of data is 100 times more than the total amount of textual information in the US Library of Congress. In CCBIO, as in most of biomedicine, acquisition of big data has become a daily routine. For instance, CCBIO's research was recently strengthened with the purchase of the Hyperion Imaging System, which takes immunohistochemistry to a new level, simultaneously measuring 35 protein markers across tissue sections by using imaging mass cytometry. Such advances give rise to hopes of scientific breakthroughs but also very practical questions about what to do with the data.

When the problems of big data hit in, one typical response is to call for help from bioinformatics, as if the bioinformaticians were a sort of Lactobacillus of the sciento-gastric ecosystem. They are not. Bioinformatics plays a key role in modern bioscience but it does not offer technical fixes and silver bullets to the challenges of big data. Unlike the digestive system, the purpose of scientific research is not to degrade its inputs but to refine and convert them: From information to knowledge; from knowledge to understanding. The secret ingredients in this process are ideas, models and thought. While the experienced bioinformatician may help expanding the repertoire of models and choosing and shaping the adequate approaches for data analysis and presentation, she or he cannot replace the need for clear scientific ideas about the purpose of the study, the hypotheses to be generated and possibly tested, the explanations to be sought, or the variables to be modelled and predicted. This predicament was anticipated already in 1973 by the philosopher Karl Popper, who warned that "too many dollars may chase too few ideas" and that "big science may destroy great science, and the publication explosion may kill ideas." (Popper 1975).

Yet, it is too late for nostalgic returns to single variables and data-low diets. In Norway, a new Centre for Digital Life was formed in 2016. The mission of this nation-wide network organization is to transform Norwegian biotechnology and life science by developing deeper interactions between bioscience on one hand and bioinformatics, engineering sciences, mathematics and exact sciences on the other. "Deeper interactions" means going beyond ordinary divisions of labour and facilitating mutual learning processes between the biological and the computational. Those who know about the biology need to learn more about the numbers, and the number crunchers need to learn about the biological systems being modelled. Indeed, the vision of Centre for Digital Life is that Norwegian biotechnology becomes transdisciplinary, in the sense that the collaborations across disciplines become so deep and so tight that the names and boundaries of disciplines become obsolete. Otherwise, the proper data digestion into real knowledge and understanding seems difficult to achieve.

CCBIO entered the Centre for Digital Life Norway as a partner in 2018. The collaborations between CCBIO bioscientists and distinguished bioinformatics groups, within as well as outside our own country, are multiplying and getting deeper and closer. CCBIO being a Centre of Excellence, we keep in mind Popper's warning that "the publication explosion may kill ideas." As we enter the next years of CCBIO, the focus should be less gastroenterology than gastronomy: Combine the use of Hyperion and our other sophisticated tools with digital and computational approaches and, importantly, time to think, in order to create data-rich and idea-rich knowledge that nourishes, inspires and enlightens. ••

REFERENCES: *Nature, 2016, "The power of big data must be harnessed for medical progress," 539:467-468. Popper, K. 1975, "The Rationality of Scientific Revolutions" (Herbert Spencer Lecture), in R. Harré (ed.), Problems of Scientific Revolution, Oxford: Oxford University Press, pp. 72–101.*

CCBIO Opinion

Text: Donald Gullberg & Arne Östman, CCBIO

The Tumor Microenvironment: Barrier or Support?

The tumor microenvironement (TME) is a complex meshwork of extracellular matrix (ECM) macromolecules filled with a variety of cells including cancer-associated fibroblasts (CAFs), blood vessel associated smooth muscle cells, pericytes and endothelial cells, mesenchymal stem cells and a variety of immune cells. The mechanisms for the autocrine-, paracrine-, mechano-, and hypoxia-dependent signaling events in CAFs in the TME varies with the tumor type, tissue, the position of cells within the tumor and the type of dynamic cell-ECM interactions that the CAFs engage in.

In most studies, the stroma is found to be tumor supportive (tumor supportive function of TME). However, two recent reports might overturn this dogma by suggesting that the TME has a restraining or suppressive effect on tumor growth (barrier function of TME) (Ozdemir et al., 2014; Rhim et al., 2014). In the first study (Ozdemir et al, 2014), conditional deletion of αSMA-expressing myofibroblasts in experimental pancreatic cancer resulted in increased tumor growth. However, some of the data might have to be re-evaluated and re-interpreted. In a study from Öhlund et al (Ohlund et al., 2017), two major types of CAFs were identified in a mouse model and in human pancreatic cancer tissue. The peritumoral CAFs expressed fibroblast activation protein (FAP) and high levels of αSMA, and were denoted myofibroblastic CAFs (myCAFs). CAFs located at further distance from tumor cells and which expressed lower levels of FAP and αSMA were named inflammatory CAFs, iCAFs. The study convincingly indicated that CAFs can change from one state to the other (myCAFs to iCAFs and vice versa) in a dynamic manner. The findings in this study might have implications for the interpretation of the Ozdemir paper. It is for example possible that ablation of all cells expressing αSMA, in addition to deleting CAFs, also delete smooth muscle cells, interfering with blood vessel function. The study from Öhlund raises the possibility that preferential deletion of myCAFs (high α-SMA expression) could have an effect different from deletion of iCAFs (low α- SMA expression).

These findings present a strong rationale for continued in-depth profiling and subclassification of CAFs. Some interesting studies have already appeared using multiplexed FACS or single cell sequencing to identify functionally distinct and marker-defined CAF subsets

(Bartoschek et al., 2018; Costa et al., 2018; Costa-Almeida et al., 2018). Ongoing studies in our own laboratories also contribute to this field. A recent study demonstrated differential prognostic associations with PDGFR-defined CAF subsets in breast cancer (Strell, 2019; Östman group). Our studies continue to indicate that PDGFalphaR and PDGFbetaR define clinically relevant CAF subsets in other tumor types. Likewise, ongoing studies of the role of integrin α11 in a breast cancer model and a squamous carcinoma model strongly suggest that integrin α11 is an interesting CAF biomarker worthy of further investigation (Primac et al., 2018).

The final word on the tumor stroma being supportive or restrictive has thus not been said yet. However, one can still be optimistic that continued studies will ultimately present yet unknown biomarker and drug target opportunities in the CAF landscape. ••

CCBIO Opinion

Text: Jean-Christophe Bourdon & Bjørn Tore Gjertsen, CCBIO

p53 Isoforms - Guardians of the Tumor-Host Interaction

In 1989, it was shown that TP53 gene mutations are frequent in human cancers and are associated with poor clinical outcome. In the 90s, it was established that cancer treatments might restore p53 activity, which in turn triggers tumor clearance. The rapid progress enticed clinicians and pharmaceutical companies to intensify their efforts and to invest heavily in translating p53 into the clinic. This worldwide effort led to the findings that p53 and its acquaintances seem to be necessary to understand the evolving landscape of cancer therapy, including examples of platinum-conjugates and PARP inhibitors in TP53 mutated ovarian cancer. Moreover, the knowledge of the p53 partner and regulator MDM2 has spawned the new drug family ubiquitin E3 ligase inhibitors. In the late 90s, the understanding of p53 sparked reasonable hopes that cancer could be beaten by the 2020s.

However, this understanding has led to no major breakthrough in cancer treatment. Moreover, the finding that the TP53 gene is alternatively spliced, and thus co-express up to 12 different p53 proteins (p53 isoforms) that regulate p53 tumor suppressive activities, have led the cancer research community to shift its interest away from p53 in the quest for new potent cancer-related genes easier to work with and translate into the clinic. The International Cancer Genome Consortium was thus created to identify, in an unbiased manner, the most frequently mutated genes in human cancers by sequencing the entire genome of 25,000 tumors derived from 25 different tissues. The results are overwhelming. TP53 emerges by far as the most frequently mutated gene in human cancers, indicating there are no alternative and easier roads to cancer treatment than to break the p53 isoform code.

The TP53 gene co-expresses, in a tissue dependent manner, up to 12 different p53 protein isoforms that regulate cell fate outcome in response to cell signals and cellular context. Cancer treatment affects p53 isoform expression, and alterations in p53 isoform expression change the cell response to treatment. It is unequivocally established that p53 protein activities are regulated by post-translational modifications induced in normal and cancer cells by multiple and concomitant intracellular and extracellular signals in response to cancer treatment, thus promoting a cell and tissue response precisely adapted to the cell signals and cellular context. Interestingly, p53 isoform expression is abnormally regulated in a wide range of human cancers. Recently, several clinical studies reported that p53 isoform expression is associated to patient outcome in various cancers. Experimentally, the co-expressed p53 isoforms orchestrate in response to cell signals genome-scale epigenetic reprogramming and gene expression leading to cell pluripotency (iPSCs, or stem cells), epithelial-to-mesenchymal transition, cell invasion, cell proliferation, cell differentiation or cell death. In addition, the p53 isoform promotes cytokine expression and secretion regulating immune cell response, angiogenesis and fibroblasts activities in the tumor stroma.

To decipher the p53 isoform code, several p53 isoform antibodies have recently been developed at the University of Dundee, and their validation in collaboration with CCBIO laboratories is currently ongoing. Hopefully, the antibodies will enable identification of patients with high risk of cancer progression and guide in the decision making of the most effective cancer therapy. Thus, p53 isoforms may open large and exciting avenues to cancer treatment. ••

CCBIO Opinion

Text: Caroline Engen, CCBIO

Precision Medicine - Lost in Translation?

Inter-individual and inter-cellular molecular diversity is associated with specific disease processes as well as with diverse life outcomes. During the last two decades, the attention of biomedical, translational and clinical research has converged towards the study of such molecular heterogeneity, in an attempt to translate precise biological understanding into meaningful clinical applications. Substantial accomplishments attributed to this approach have resulted in the development of medical strategies characterized by incorporation of molecular characteristics in disease categorization, prognostication, clinical decision-making and therapeutic development. The traction of these strategies has been enforced by rapid technological advancements, as well as broad financial and political support. Novel relationships between stakeholders have developed and matured, resulting in the emergence of a co-produced imaginary; precision medicine. This imaginary is not confined by clinical applicability but is a compound concept built on ambitions and visions of what can be achieved through increased precision in medical care; visions of a future with far less disease, suffering and death. Founded on these promises, techno-scientific optimism and assumptions of benefit, a profound transformation of health care practices, health care delivery systems, knowledge generation, policy and regulatory strategies have been set in motion, gradually translating concept to reality.

Importantly, the imaginary of precision medicine serves a democratic and ethically grounded goal; improving life quality and population health outcomes. The utility, validity and legitimacy of precision medicine should therefore be evaluated and deliberated upon in this explicit context. Although observational and experimental experience suggests that precise medical strategies are feasible and sometimes efficient, the political as well as scientific discourse of precision medicine is predominantly built on visions rather than realizations. This is accentuated by estimates suggesting that less than 5% of the American cancer patient population currently benefit from precision medicine (Marquart, Chen et al. 2018), and that most recent European market approved oncologic agents either fail to display, or demonstrate only marginal improvements in survival time or quality of life (Davis, Naci et al. 2017).

It is appealing to attribute these sobering results to lack of knowledge, and shortage of clinical tools and targeted agents. It is, however, also possible that the expectations of precision medicine fundamentally fall short due to its lack of true inherent potential. The investigational objectives of CCBIO exceed the traditional molecular emphasis of precision medicine and focus on an expanding biological understanding of cancer cells' contextual relationships. CCBIO researchers have repeatedly demonstrated that interactions amongst cells and between cells and their physical and biochemical microenvironment influence emerging cellular properties and shape disease trajectories. This dynamic interplay has further been shown to impact both therapeutic responses and disease outcome. Cancer, as portrayed by CCBIO researchers, is an evolving relational process; profoundly imprecise in descriptive and functional terms. With this in mind, the pressing question is whether precision medicine can ever be precise enough to truly provide benefit in a public health perspective, technical and financial constrains set a side.

As researchers and experimentalists, our mandate is to generate and disseminate knowledge to inform democratic processes. Repercussions of the dissonance between investments, expectations and the current reality of precision medicine are materializing, and perhaps righteously negatively influencing the legitimacy of both precision medicine and policy makers. Our constructive contribution in this discourse should include management of expectations and disclosure of limitations and uncertainty. We cannot know if precision medicine will provide sizable benefits on a population level in comparison to alternatives. We do however know, with great confidence, that precision medicine will not solve the problem of suffering and mortality. When overpromises are made, it is in our interest to modify the "great expectations"; to protect the legitimacy of our work and our investments. ••

Davis, C., H. Naci, E. Gurpinar, E. Poplavska, A. Pinto and A. Aggarwal (2017). "Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13." BMJ 359: j4530. Marquart, J., E. Y. Chen and V. Prasad (2018). "Moving Precision Oncology Forward Amid Myths and Misconceptions-Reply." JAMA Oncol 4(12): 1790.

CCBIO Opinion:
Text: Yves Aubert, CCBIO Research Advisor

Integration of Innovation

Importance of impact, innovation, and IPR

Until recently, a typical research project would end with the researcher writing up project results and publishing the findings in a peer-reviewed journal. At CCBIO, we understand that the creation and publication of project results are important milestones, but not the end of the journey. We have anticipated recent research and innovation policy changes at the national and European levels that push for academic research to create greater societal and commercial value. Such demands also hold true for the Norwegian Centers of Excellence, despite their strong focus on research.

The key word here – used by both the Research Council of Norway (RCN) and by the European Commission – is the generation of impact. Indeed, in 2019, scientific and societal impact of proposed research projects will for the first time be evaluated in all project proposals submitted to the RCN, regardless of program or call type. The generation of impact implies that research results need to be communicated to the public, systematically disseminated to all relevant end-users, and made available to be used by these end-user groups.

Innovation is characterized by a similar principle. Innovation is not merely an invention, or the creation of something novel that goes beyond the state-of-the-art, but is rather an invention that

is linked to an active process that ultimately turns the invention into a novel product or service which is then made available to the end-users. A typical, but not only, example for such a process is commercialization.

Successful innovation often depends on the securing of intellectual property rights (IPR), and the knowledge that the academic research, including potential future commercial exploitation of the research results, can be performed without infringing the IPR of someone else (freedom to operate). It is crucial that all researchers are informed about the rules surrounding IPR, such as the rule that a patent can only be granted for novel products, processes or methods if they have not yet entered the public domain. Any scientific publication, or presentation at a conference, means that the presented information has entered the public domain and is thereby no longer eligible for IPR protection. Ergo, patent filing prior to publication is essential, at least in Europe (there are differences to this rule in e.g. the USA), but often neglected by academia. The reality is that without IPR secured, commercialization in the biomedical field becomes nearly impossible, meaning that the academic research output will ultimately fail to reach the intended end-users (e.g., patients and clinicians) in significant numbers, outside the clinical trial setting.

How CCBIO creates impact: ongoing activities

Research performed at CCBIO carries much relevance to millions of patients suffering from different forms of cancer, to clinicians that are waiting for better diagnostic tools and better tailored treatment options to offer to their patients, to the family members that are so greatly affected by the ailment of their loved ones, and not least to the nations' health economies which are burdened by the loss of productivity and exorbitant treatment costs. The potential for societal impact of CCBIO is thus immense.

As a Center of Excellence, CCBIO is predestined to impact its core academic fields (tumor microenvironment, cancer biomarkers) through high impact publications, quality researcher education, and the dissemination and communication of new knowledge through public and academic channels.

In the years past, CCBIO has successfully managed to produce scientific output with significant impact on its scientific environment, and made it available through textbooks (Akslen & Watnick, 2017; Blanchard & Strand, 2017) and peer-reviewed publications. We have continued these activities in 2018 (see list of publications) and have been in an active dialogue with the interested public at different venues, including appearances at a public panel discussion on the "future of cancer treatment" (Litteraturhuset Bergen), contributions to a feature program on the future of the healthcare system in Norway by the national broadcasting station NRK, and through the CCBIO seminar series.

A core strength of CCBIO, recognized by both the mid-term evaluation panel and the center's international scientific advisory board, has been the center's ability to rapidly translate findings from basic research to clinical application through the initiation of multi-center clinical trials, implemented in collaboration with Haukeland University Hospital, and through commercial R&D efforts at the CCBIO partner companies with links to CCBIO PIs, BerGenBio (PI Lorens), Alden Cancer Therapy II (PIs Kalland and Gjertsen), and KinN Therapeutics (PIs Gjertsen and McCormack).

From its conception, CCBIO has put strong emphasis on ethical, economic and societal aspects of cancer research. CCBIO has reaffirmed its dedication to responsible research and innovation and has appointed Roger Strand as main PI and leader of a task group that also include Associate Investigators John Cairns and Ole Frithjof Norheim, to investigate the developments and expectations of personalized cancer medicine from the perspectives of political, ethical and societal impacts.

How CCBIO creates impact: future activities

We will continue with our core task of producing excellent research, and we will renew our effort to ensure that the potential scientific and societal impacts derived from our research will be maximized. To achieve this goal, we set a number of activities into motion:

A) Better education of scientific personnel on IPR. We recognize that the understanding of and literacy in IP-related matters is crucial to make new medical discoveries available to cancer patients through the process of commercialization. In January 2019, in partnership with the Medical Faculty of the University of Bergen, VIS (formerly BTO, the Bergen Technology Transfer Office), and Digital Life Norway, CCBIO will contribute towards a one-day and highly visible IPR seminar. We will continue this activity and reach out to researchers to provide relevant information on IP and IPR.

B) Establish an internal IP management and innovation plan. An IP management and innovation plan will not only outline background and foreground IP of collaborative research projects between internal CCBIO researchers, and with external project partners from academia and industry, but also allow to better track the innovation process of CCBIO projects and determine potential gaps in the process. This in turn will allow for timely actions to be taken to assure that the research results will deliver real-life solutions for patients and clinicians.

C) Integration of academic innovation with industry. We understand that the development of novel cancer biomarkers will ultimately depend on thriving partnerships with industrial partners. For this purpose, CCBIO will actively continue to reach out to potential industry partners to establish an even more efficient R&D process from biomarker discovery to clinically available diagnostic, prognostic or predictive tools. ••

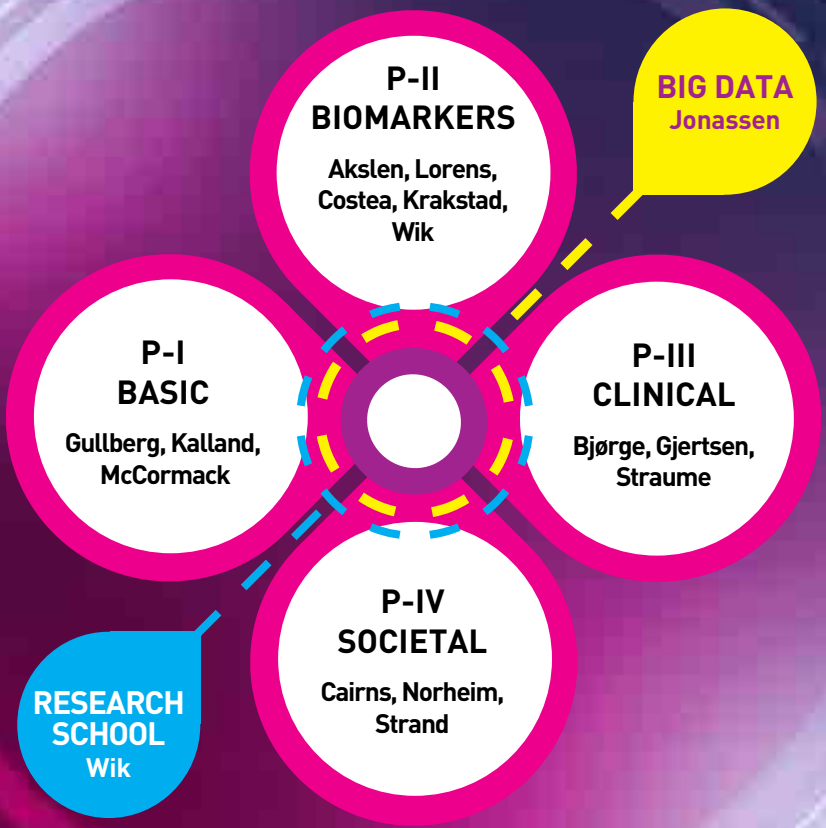
Organization of the Center

CCBIO is organized across seven departments and four faculties at the University of Bergen. Its main activities, with PIs, AIs, and most of the other staff, are located at the Faculty of Medicine´s departments: Department of Clinical Medicine, Department of Clinical Science, and Department of Biomedicine.

The majority of CCBIO´s PIs hold positions and funding at Haukeland University Hospital. 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 four integrated research programs with associated teams (basic studies, biomarker exploration and validation studies, clinical studies, and societal studies), all supported by bioinformatics resources (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 scientific and administrative 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 strategy seminar bi-annually (1-2 days). The monthly meetings and the bi-annual strategy seminars are important platforms for communication and increased collaboration within CCBIO.

Management group
In 2018, CCBIO was managed by the director, Professor Lars A. Akslen, the co-director, Professor Bjørn Tore Gjertsen, and Ragna Breines as administrative leader until Geir Olav Løken returned to his position in August 2018



PRECLINICAL MODELS
Animals and cell models
MIC - PROBE - FLOW
Animal imaging

BIOMARKERS
Biobanks - Registries
Immunohistochemistry
Microarray - Bioinformatics
Imaging mass cytometry

CLINICAL STUDIES
Multicenter studies
Clinical Trials Unit HUH
Infrastructure and logistics

after a one year leave. The management group is assisted by four finance officers, a web and newsletter editor, the faculty communications officers and a 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 as a matrix structure 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.• •

In their 2018 report, the SAB stated that CCBIO has done an outstanding job of building the faculty, leadership, infrastructure, research, clinical trials, and education programs necessary for a true center of excellence.

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 convenes once a year for a full day meeting with the CCBIO PIs and associate investigators, mostly following the CCBIO Annual Symposium. The SAB's feedback has been of great inspiration and utility to CCBIO and for every SAB meeting, CCBIO provides the SAB a report on the response to their recommendations.

In their 2018 report, the SAB stated that CCBIO has done an outstanding job of building the faculty, leadership, infrastructure, research, clinical trials, and education programs necessary for a true center of excellence. The SAB also stated that after a successful completion of the first half of the funding period and a very positive mid-term evaluation, CCBIO is now in a good position to take on additional challenges for the second funding period. The SAB's overarching recommendation was for CCBIO to narrow its priorities, focusing on what CCBIO should deliver at the end of its funding cycle in 2023, as well as how to position itself for the future beyond 2023.

CCBIO was encouraged to continue its inclusion of young faculty to improve its prospects for the future, including an improved gender balance at the senior level. The SAB also stated that CCBIO's strategy of recruiting adjunct international researchers should be continued and widened, focusing specifically on recruiting bioinformaticians to affiliated positions, and to accelerate the adoption of bioinformatics and other tools to process big data into CCBIO's discovery, validation and clinical implementation of novel biomarkers.

The SAB characterized the discovery of new biomarkers as one of CCBIO's major strengths and recommends incorporating its biomarkers even more strongly into clinical trials in order to maximize utility for society. It also acclaimed CCBIO's emphasis on liquid biomarkers and encouraged CCBIO to focus more intently on the validation and clinical adoption of a subset of these biomarkers. The increase in the number of clinical trials performed within the CCBIO context was acclaimed by the SAB, and CCBIO was recommended to contribute towards improvements of the routine biomarker collection infrastructure in its vicinity. CCBIO's industry interactions is seen by the SAB as a strong basis for further development as well as recruitment of industry-associated advisors or adjunct faculty.

The SAB lauds CCBIO's effort within societal projects (ethics, economics, and priorities related to novel cancer biomarkers) for working with the outside community through its education and outreach programs. It characterized the inclusion of ELSA lectures at the Symposium as a great success as it stimulated much thinking and discussion on these topics. ••

Carl-Henrik Heldin is the chairman of CCBIO's SAB and is professor at Uppsala University, Sweden, and chairman of the Nobel Foundation.

Ate van der Zee is professor of gynecological oncology and vice chair 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.

Scientific Activities and Progress

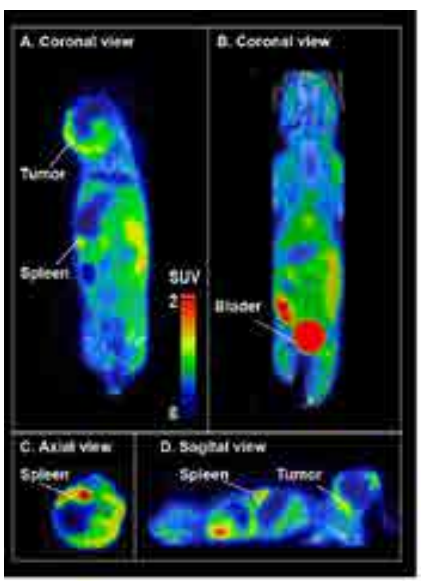
CCBIO has a focus on biomarkers of tumor-microenvironment interactions and plasticity programs in primary and metastatic cancers, and how these can define aggressive tumor phenotypes and predict tumor progression and treatment response. Studies on societal aspects, such as ethics and economics, represent an integrated part of CCBIO.

During 2018, CCBIO entered its second 5-year term, and the organization was modified to better reflect its current research landscape. We now have four programs and teams of principal and associate investigators, working on basic studies of cancer mechanisms (Team I), discovery and validation of cancer biomarkers in human tissues (Team II), clinical studies and trials (Team III) and societal studies (Team IV). These four teams are supported by bioinformatics resources, coordinated by Associate Investigator Inge Jonassen. Increased internal and external collaboration and networking is taking place. In CCBIO, research is combined with science education and science communication. The ambition is to create an organic and well functioning science culture. During 2018, the CCBIO Research School for Cancer Studies activity reached a peak. Several efforts and initiatives within CCBIO are now up and running. The projects are spanning from tumor microenvironment biology including matrix mechanisms and tumor-immune interactions, through exploration of simple and complex biomarkers, to clinical trials with targeted biomarker panels using liquid biopsies and single cell analysis. For the coming years, our initiative in deep tissue profilling by imaging mass cytometry (established 2018) is expected to have significant impact.

In **TEAM I,** the area for basic studies, many projects are focusing on how tumor cells interact with the surrounding microenvironment, by activation of angiogenesis, immune cell participation, fibroblast and matrix involvement, favouring tumor growth and metastatic spread.

According to a drug repurposing strategy, two approaches were performed (**Kalland group**). First, 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., Nature Chem Biol 2018). Second, panels of purified compounds from plants used in traditional Chinese medicine (TCM) identified potential STAT3 inhibitors (Hua et al., 2018). Notably, ß-catenin and STAT signaling are key pathways that determine pro- and anti-inflammatory decisions of the immune system.

The **McCormack group** has worked on the development of non-genotoxic therapies that activate wild-type p53 in tumors by DHODH inhibition (Ladds et al. Nature Comm, 2018), by screening over 100 small-molecules activating p53 in cells. The team proposes a strategy to promote cancer cell killing by p53 instead of its reversible cell

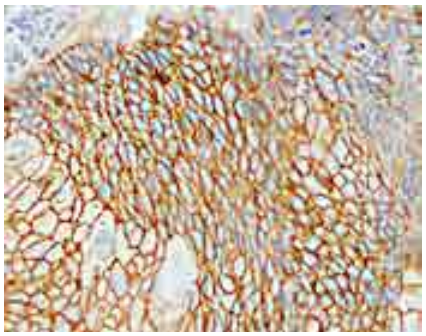


cycle arresting effect. The group also reported that blockage of autophagic flux by tenovins is necessary to eliminate melanoma cells that survive B-Raf inhibition (Ladds et al, 2018). This observation is of great relevance as relapse and resistance are frequently observed in cancer patients treated with B-Raf inhibitors. The group has established a wide range of PDX-models combined with various imaging strategies.

The **Gullberg group** has mainly been working on the characterization of novel integrin α11 function blocking antibodies and a new mouse model to study the role of this microenvironment matrix in different cancers.

In **TEAM II**, several 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 and final outcome. In breast cancer, the **Akslen group**, including **Associate Investigator Wik**, has established a deep tissue profiling initiative during the last couple of years, and now focus on proteomics studies of breast cancer subtypes, on bulk tumor tissue as well as on laser capture microdissected samples enabling profiling of the tumor cell and microenvironment compartments separately (Finne et al., in prep). In addition, cell lines and human samples are studied for hypoxia induced protein responses and metabolic reprogramming, indicating marked changes between luminal-like (hormone receptor positive) and basal-like (hormone receptor negative) breast cancer subtypes (Kjølle et al., in prep). Among others, detailed studies of IL8 and Nestin pathways, using CRISPR technology, are ongoing. Studies of microenvironment biology in breast cancer, including co-regulation of vascular, immunologic and neurogenic responses, are ongoing (Wik et al, in prep; Aziz et al, in prep). The group collaborates with the Cancer Registry of Norway on national breast cancer data and also on radiologic imaging

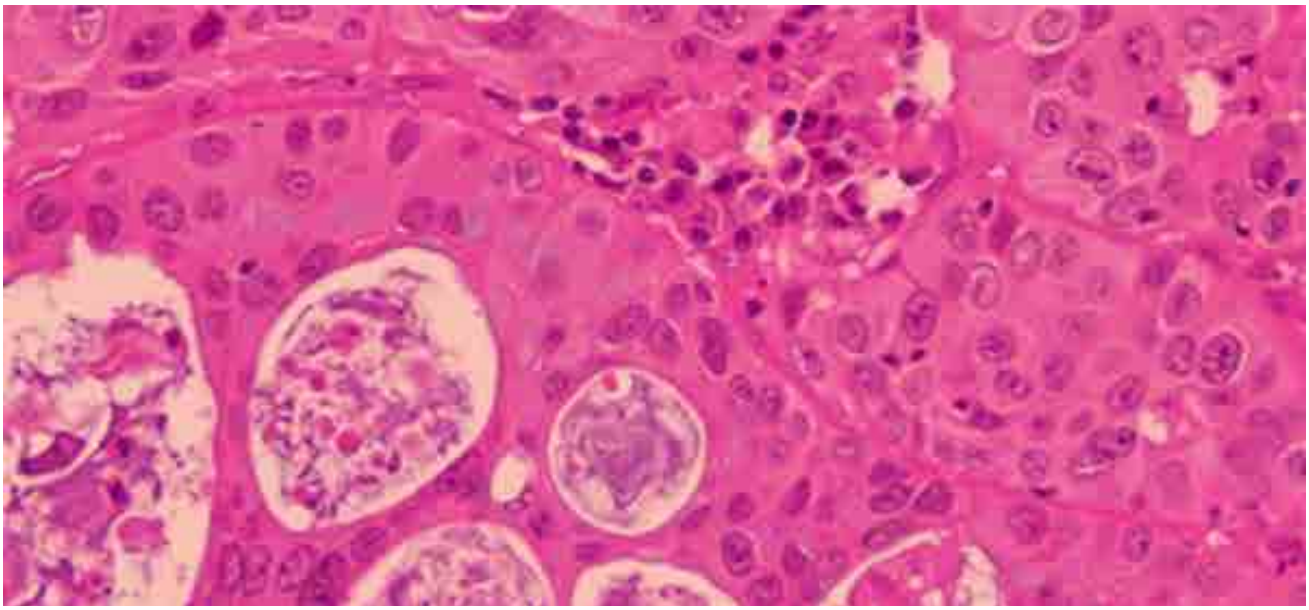
The complexity of the tumor microenvironment necessitates high dimensional single cell analysis approaches.



biomarkers of breast tissue and malignant tumors.

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 and interactions at the tumor-immune interface (**Lorens group**, and collaboration with CCBIO Affiliated Professor Brekken). Notably, 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 (Ludvik et al., 2018). Axl inhibition drove tumor cell differentiation and reversed gemcitabine resistance mechanisms and potentiated an immune stimulatory microenvironment by targeting immune suppressive myeloid cell types. Hence Axl targeting affects pathways that improve treatment efficacy. The complexity of the tumor microenvironment necessitates high dimensional single cell analysis approaches. Together with CCBIO Affiliated Professor LaBarge and international collaborators, the Lorens group reported new technologies that allow multidimensional mapping of phenotypic plasticity (Pelissier Vatter et al., 2018; Jokela et al., 2018). The Brekken-Lorens collaboration has documented a role of the Axl receptor in cancer therapy failure. This resulted in a recent clinical translation of novel Axl targeting agents e.g. bemcentinib (BGB324), to treat pancreatic cancer (NCT03649321; NCT03536208). Deep tissue profiling technology (by imaging mass cytometry) will be performed on patient biopsy samples using the CCBIO platform, to measure phenotypic and spatial organizational features within the tumor microenvironment that determine outcome to cancer therapy.

In studies of gynecologic cancers (**Krakstad group**), protein expression differences between primary tumors and their metastases, as well as the prognostic value, have been published. The group has established the usefulness of ASRGL1 (Fonnes et al, 2018) as a prognostic marker in endometrial cancer. Further, the group has continued its focus on the role of hormone receptors in endometrial cancers. The MOMATEC2 study (NCT02543710), a phase 4 implementation trial for validation of ER/PR status as a stratifier

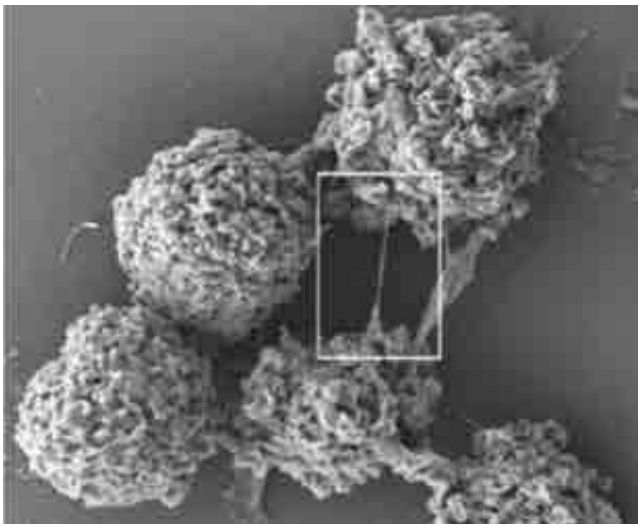


for lymphadenectomy in endometrial cancer, is ongoing. The influence of obesity has been studied, and proteomic profiling of tumor tissue showed differences between obese and non-obese patients. The group has also established novel PDX models for endometrial cancer for future studies.

The **Costea group** studies epithelial-mesenchymal interactions in oral and vulvar squamous cell carcinoma, with particular focus on metabolic reprogramming of carcinoma associated fibroblasts, the association with genetic alterations including HPV and their role for tumor progression.

In **TEAM III**, the main focus of the **Gjertsen group** has been single cell profiling of leukemia treated with novel targeted therapy and conventional therapy, particularly related to clinical trials, with biomarker studies. In AML, a wide phosphoprotein screen was performed using phospho-proteinenriching columns and differential gel electrophoresis (Forthun et al., 2018). 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. Two new projects have been established in 2018, one for development of CSF1R/FLT3 inhibitor and one on repurposing quinacrine and valproic acid for use in leukemia. Both projects aim to develop single cell signaling profiling as a biomarker for indentifying responders and non-responders. The CSF1R signaling system is essential in stromal cells, and inhibition of CSF1R may represent an alternative or co-existing resistance mechanism to Axl. The group presented data showing tolerance of the new Axl inhibitor bemcentinib, effect on cellular signaling by mass cytometry, and how single cell profiling can be used to monitor early responses in AML (major hematology and cancer meetings ASCO, EHA, ASH). The group is active in the p53 field, and they are currently working on how cancer-related signal transduction systems modulate isoforms of p53, representing a novel mechanism of therapy.

A national academic trial (CCBIO based) combining anti-Axl treatment with immunotherapy is ongoing (**Straume group**), in patients with advanced non-resectable (Stage IIIc) or metastatic (Stage IV) melanoma. The 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. Further, a national interventional study in patients with unresectable or metastatic melanoma (IPI4; ipilimumab) is being analyzed, and the goal is to identify predictive value



of VEGF related biomarkers. Results on potentially predictive biomarkers in clinical trials of melanoma and renal cancer were published (Schuster et al, 2018; Pilskog et al., 2018).

The dendritic cell based cryo-immunotherapy trial on prostate cancer (CryoIT Phase I) is progressing well (**Kalland and Gjertsen groups**). 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).

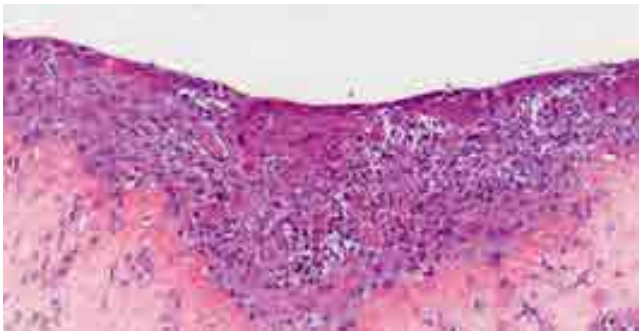
The **Bjørge group** is actively participating in novel multicenter trials with translational research. The recruitment of patients for the Horizon 2020-funded project FORECEE was completed in early fall 2018, and more than 500 women were included from the Women's Clinic, Haukeland University Hospital, Bergen. A presentation of the concept of epigenetic testing was published in early 2018 (Widschwendter et al., Nature Rev Clin Oncol 2018). The group's two early-phase investigator-initiated studies, IMPACT and INFLUENCE, are ongoing. The epigenetic profiling of the patient cohorts has been undertaken and analyzed (to be reported). A profiling of the isoform landscape of high-grade serous ovarian and uterine cancers was reported (Bischof et al., 2018), indicating that the expression is heterogeneous and dominated by Δ133p53. The data suggest the use of isoform data for prognostication.

In **TEAM IV**, the projects on ethics and economics of biomarker based therapy are expanding and are being integrated in the recently established clinical trials. 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 the improvement of cancer diagnostics and therapies and in medical innovation. 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 and has now established a team structure led by **Strand**, by improved integration into one interdisciplinary humanities and social science program to study the opportunities and challenges of precision cancer medicine. The team will deepen the collaboration with CCBIO cancer researchers to promote the integration of ELSA perspectives and RRI into practice. Furthermore, the team 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.

The **Strand 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. The group is well on the way to create a joint program with CCBIO ethicists (**Norheim group**) and economists (**Cairns group**). In 2018, the ELSA group's anthology "Cancer Biomarkers: Ethics, Economics and Society" (Blanchard & Strand, eds) was published in a second and lightly revised edition.

The primary health economic projects (**Cairns group**) are the PhDs by Kelly Seo (Cost-effectiveness modelling of predictive biomarkers in targeted oncology therapies) and Ana Beatriz Luis (Incentives for developing new cancer biomarkers and targeted therapies). The candidates have recently collaborated on a paper assessing the impact of cancer biomarkers on health outcomes in Norway. Their results suggest that biomarker tests improve health by ensuring that the right treatment is given to the right patient and that the effect is stronger for cancer types for which fewer drugs are available. The



two health economics PhDs are well-advanced and should be completed over the next year. Plans are currently being developed for a new PhD examining the potential role of observational data in the evaluation of cancer biomarkers to inform priority setting. Further, it is intended to build on the cost-effectiveness modeling in Seo's thesis by developing economic evaluation of specific cancer biomarkers of central interest to CCBIO. In addition, planning is underway for the next CCBIO903 course to be held December 2019 and January 2020. A collaborative project on priority setting is planned to exploit the strengths and common interests of the Ethics, Economics and ELSA research groups.

In the **Norheim group**, one aim has been to methodically map out the role of patient age in clinical decision making in cancer care. The group's findings suggest that patient age is widely used, directly or indirectly – and consciously or unconsciously – to guide clinical decisions (Tranvåg et al., 2018). Further work will investigate how information from cancer biomarkers will blend into this decision-making process and if, as predicted by many, it will lead to fairer priority setting decisions.

Altogether in **TEAMS I-IV**, a range of projects and supporting activities have been established during the first CCBIO term and continue into the second term. In addition to many publications and also books presented by CCBIO, several educational activities have been established, and we continue to reflect on the core characteristics of scientific excellence and the transition to real life impact. ••

Societal Impact- Normal and Extraordinary

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 in 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.

In previous annual reports, we have reflected on the implications of this insight in terms of the need for responsible cancer research that anticipates and reflects on issues of justice and fairness. Since the inception of CCBIO in 2013, we have witnessed an increased level of attention to impact measurements and metrics in research funding organizations (such as our funder, the Research Council of Norway) and research performing organizations such as our own university. Sivertsen and Meijer (2018) make the useful distinction between normal and extraordinary impact. They define normal impact as "more-or-less active, productive and responsible interactions between (units of) research organizations according to their purposes and aims in society" (p.1). In our case, the normal impact of CCBIO consists in our steadily accumulating contributions to the scientific literature along the axis from basic studies to more translational projects, our close interaction with hospitals in the design and execution of clinical trials and the uptake of new medical knowledge and technology in the clinic, and our interactions with industry (e.g. the Axl story). An important part of the normal impact is also our continuous and extensive dissemination towards and interaction with civil society, and our ongoing exchanges with Norwegian health policy-makers, in particular around the visions and "great expectations" of personalized medicine in contrast to quite significant conceptual and practical challenges.

Yet, what is often highlighted and sought for in current frenzies for impact, is what Sivertsen and Meijer (2018) call "extraordinary impact": rare incidences with the "wow" factor and immediate or widespread implications for society – a revolutionary "cure", a paper in Nature, Science or perhaps the Lancet, a novel product with huge revenues. Sivertsen and Meijer observe that extraordinary impact is often based on serendipity, and they warn that long-term impact may be compromised if research environments become too focused on hunting or wishing for the extraordinary. We agree with their analysis. It is wise to distinguish between visibility and impact. Visibility and sensational developments have of course their rightful place, but their position is on top of solid, normal, long-term work. This being said, CCBIO is also a research environment for the testing of medium to high-risk ideas, as is proper for a center of excellence, and our tolerance to risk will not decrease in the second period towards 2023. ••

REFERENCE: *G. Sivertsen & I. Meijer (2018). Evaluating and improving research-society relations: The role of normal and extraordinary impact, R-Quest Policy Brief No. 3, p. 1-5, URL https://www.r-quest.no/wp-content/uploads/2019/01/R-QUEST-Policy-Brief-3.pdf*

Research Teams and Programs

For the second term, the organization of CCBIO has been modified to reflect the current research activities. We now have 4 teams and corresponding project areas: basic studies of tumor-microenvironment interactions (Team 1), exploration and validation of cancer biomarkers in human tissues (Team 2), clinical studies and trials (Team 3), and societal studies including projects on ethics, economics and priorities (Team 4). On top of this, the four programs are supported by resources on bioinformatics and processing of big data.

Rolf Reed is now a strategic advisor. Increased collaboration within CCBIO, between the different teams and investigators, has taken place over the years.

Team 1

Mechanisms of Tumor-Microenvironment Interactions

The aim of this program is to examine how tumor cells interact with the surrounding and supporting microenvironment with different cell types like fibroblasts, immune cells, vascular cells and stem cells embedded in the complex extracellular matrix. This team consists of the Principal Investigators Kalland, Gullberg and McCormack and their groups.

DONALD GULLBERG

Research focus
The research is focused on work related to integrin alpha11beta1. This is a collagen receptor with a number of features suggesting that it is a key molecule in tumor fibrosis. The group has performed detailed molecular studies of cell-collagen interactions *in vitro* and *in vivo* and developed a number of reagents enabling these studies.

Projects
The CCBIO projects deal with the role of integrin alpha11 in tumor stroma by:

• Generating new animal models to conditionally inactivate genes in an integrin alpha11-specific manner. 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).

•Using functional blocking antibodies to human alpha11 integrin to analyze alpha11 expression and function in cancer associated fibroblasts (CAFs) in different tumor types in both *in vitro* and *in vivo* assays.

• Studying squamous carcinoma using integrin alpha11 integrin knockout mice. This is a collaborative project with CCBIO-affiliated researcher Ritva Heljasvaara.

Important results
Novel animal model: 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 is ongoing.

During 2018, ITGA11-Cre activity in the mouse strain has been determined by crossing the ITGA11-Cre mice with a reporter mouse strain, Rosa 26R, so that Cre activity is monitored as beta-galactosidase activity. So far, ITGA11-Cre activity has been characterized by X-gal staining in mouse embryos, in isolated mouse embryonic fibroblasts and in fibrotic mouse hearts. Beta-galactosidase expression has been analyzed by Western blotting in parallel and in adult mouse tissue samples.

Novel antibodies: Function blocking monoclonal antibodies (Mabs), as well as Mabs suitable for biomarker studies on fixed tissues, are being characterized in a variety of ways including functional assays on cells as well as by immunohistochemical studies of human tissue samples.

During 2018, all antibodies have been sequenced. Epitope mapping using chimeric alpha11/alpha2 integrin swapping cDNA constructs stably expressed in C2C12 cells has been completed. Epitope mapping using alpha11 deletion constructs expressed in HEK293 cells are ongoing. The function blocking assays have been extended to include CAFs from different tumor types, in fibrosis and in spheroid assays (manuscript in prep.)

Future plans
The characterization of the ITGA11-Cre mouse strain will continue to include analysis of ITGA11-Cre expression in skin wounds (collaborator in Cologne) as well as in tumor stroma (collaborator in Toronto).

Epitope mapping of Mabs will continue in 2019 and will also include assays to determine mode of action of function blocking antibodies (direct or allosteric inhibition) and possible overlap of epitopes (competitive ELISA assay).

Current challenges in the field
In tumor and tissue fibrosis there is currently a focus on understanding the role of different subsets of fibroblasts/myofibroblasts/CAFs. In addition to descriptive studies defining biomarker repertoire of subsets of stromal cells, there is also a great interest in understanding the molecular mechanism of action of pro-fibrotic mechanisms. A major challenge will be to identify the details of these mechanisms in various CAF subsets in different tumor types.

CCBIO focus in the coming years
The group hopes to create a humanized integrin alpha11 mouse model to be able to do *in vivo* assays for tissue and tumor fibrosis, using the generated and characterized function blocking Mabs. They also hope to validate the usefulness of the ITGA11-Cre by deleting floxed genes in an alpha11-specific manner in both tissue and tumor fibrosis models. ••

GROUP MEMBERS:

Gullberg, Donald, PhD, professor, group leader
Kusche-Gullberg, Marion, PhD, professor
Alam, Jahedul, MSc, PhD candidate
Sembajwe, Lawrence Fred, PhD candidate
Moses, Musiime, MSc, PhD candidate
Grønning, Mona, chief engineer
Lu, Ning, PhD, senior laboratory engineer
Ben Mohamed, Fatima, master student

KARL-HENNING KALLAND

Research focus
The Prostate Cancer Therapy Research Group continues both its drug discovery and developmental program and the clinical trial of dendritic cell-based cryo-immunotherapy (CryoIT) against cancer.

Projects
The repurposing strategy and screening of FDA-approved drug panels resulted in a publication in Nature Chemical Biology (2018). A broad methodological repertoire identified compounds that inhibited oncogenic β-catenin signaling and revealed both the molecular target and the molecular mechanisms of β-catenin inhibition by the compound nitazoxanide. The alternative approach to screen panels of purified compounds from plants used in traditional Chinese medicine (TCM) identified potential STAT3 inhibitors. Further investigation of STAT3 inhibitors is ongoing.

It is important to take into consideration how a drug affects different cell types of the tissue microenvironment. It is not sufficient that the drug inhibits oncogenic signaling in cancer cells. It turns out that β-catenin signaling and STAT signaling are key pathways that determine pro- and anti-inflammatory decisions of the immune system. The group's recent work with human monocyte-derived dendritic cells emphasizes the need to control pro-inflammatory differentiation of therapeutic cells and the potential of β-catenin regulation. This work is an important aspect of the ongoing development of next generation CryoIT (cryo-immunotherapy).

Important results
The general conclusion of interim data of the first 13 patients is that CryoIT (ongoing clinical trial) is safe and has a good tolerance profile; serious autoimmune adverse events were not observed. This is encouraging since autoimmune side effects represent a difficult problem with immune checkpoint inhibitors. Radiological examinations of metastatic tumors showed that 5 out of 13 patients exhibited stable disease and another 3 patients had a mixed response according to different radiological modalities and RECIST criteria.

Research biobank data have provided additional information. Circulating tumor cells (CTCs) in the blood have been analyzed in collaboration with Professors Klaus Pantel and Sabine Riethdorf in Hamburg. In several patients, CTCs were detected in the blood before CryoIT but disappeared following treatment, suggesting beneficial effect on metastatic processes.

Ultradeep TCR sequencing (TCR-seq) showed robust generation of new immunity in all investigated patients within 2 weeks after CryoIT. This technique shows that specific T-cell clones (clonotypes) appeared and expanded significantly following CryoIT. The magnitude of the CryoIT immune response (number of new T-cell clones and percentage of all T-cells in the blood) compared very favorably with other published clinical trials with TCR-seq data.

The plan is to conclude the phase I clinical trial of metastatic prostate cancer in 2019 with the 18 patients presently treated with CryoIT.

Current challenges in the field
Current immune-oncology has not harnessed the full potential of therapeutic immune cells. More potent and robust production of pro-inflammatory dendritic cells and better quality control and better biomarkers are some of the challenges.

CCBIO focus in the coming years
Next generation dendritic cell-based cancer treatment is developed. Improved high throughput *in vitro* modeling of the tissue microenvironment is important, and organoid culture technology and co-cultures with immune cells may increase the capacity and relevance of drug testing. Investigation continues of immunogenic cell death and drug-mediated control of selected signal transduction pathways in order to generate robust and potent pro-inflammatory immune cells. ••

GROUP MEMBERS:

Kalland, Karl-Henning, MD, PhD, professor, group leader
Øyan, Anne Margrete, MS, PhD, senior scientist
Azeem, Waqas, PhD, postdoc
Hua, Yaping, MS, PhD candidate
Bakke, Ragnhild Maukon, medical student
Hoang, Hua My, research technician (50%)

EMMET MCCORMACK

Research focus
The 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 hematological 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 modeling.

• PreLIM focuses on the development of new preclinical models of leukemia and lymphomas in the development of novel targeted therapies and immune therapies, and exploration of microenvironmental factors critical to disease development and emergence of resistant clones.

• Through 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 synergized in AML, in addition to the development of novel models of MDS, and an exciting combination of small molecule inhibitors for MCL which is currently under review. INOvA purchased the first preclinical system for fluorescence-guided surgery of cancer. This equipment will aid resolution of malignant tissue from normal tissue and should aid the easier visualization of metastasis, critical in the surgical resection of gynecological cancers. A number of novel imaging biomarkers are being investigated for non-invasive imaging of gynecological cancers.

Future plans
To aid swift clinical translation, the group is 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 and mammary carcinoma is anticipated in 2019, providing a novel strategy for veterinary oncology care and a unique opportunity to translate observations in companion animals to the clinic.

CCBIO focus in the coming years
The group will be focusing on development of relevant preclinical models and imaging modalities that will impact the lives of patients. ••

GROUP MEMBERS:

Senior researchers:
McCormack, Emmet, PhD, professor, group leader
Kotopoulis, Spiros, PhD, senior researcher
Bredholt, Geir, PhD, researcher
Fonnes, Tina, cand.med.vet., researcher
Leitch, Calum, MSc, researcher
Langer, Anika, PhD, researcher
Gullaksen, Stein-Erik, MSc, PhD

Technical staff:
Fandalyuk, Zinayida, MSc, staff engineer, lab manager
Fosse, Vibeke, DVM, veterinarian
Popa, Mihaela Lucia, DVM, veterinarian
Safont, Mireia Mayoral, BSc, staff engineer
Thodesen, Elisa Ulvøen, MSc, staff engineer
Eriksen, May Gjerstad, MSc, staff engineer
Karlsen, Ida, MSc, staff engineer
de Montlaur, Constance de Villardi, PhD, staff engineer
Xing, Zhe, PhD, DDS, MMed, staff engineer

Postdoctoral fellows:
Gelebart, Pascal, PhD
de Garibay, Gorka Ruiz, PhD

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

Master students:
Guldberg, Erik Andreas, BSc
Lam, Christina, BSc
Rozmus, Ezekiel Richard, BSc
Sundøy, Silje Maria, BSc


2016-08
12GES13

Team 2

Exploration and Validation of Cancer Biomarkers

The aim of this program is to explore and validate different classes of biomarkers in tissue samples from human patient cohorts. The studies map associations with clinico-pathologic phenotypes as well as prognostic and potentially predictive properties. This team consists of the Principal Investigators Akslen (CCBIO director) and Lorens and their groups, and the Associate Investigators Krakstad, Costea and Wik.

LARS A. AKSLEN

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

Projects
- Proteomics portraits of breast cancer subtypes stratified by tumor cell and microenvironment compartments.
- Markers of neuro-angiogenic phenotypes in breast cancer and associations with immune responses and molecular phenotypes.
- Role of Nestin as a marker of BRCA1-related, basal-like and aggressive breast cancer subtypes.

Important results
Proteomic profiling of laser capture microdissected breast cancer tissues has been performed, separating the cancer cell and microenvironment compartments, and results have been compared with findings from bulk tissue analysis. Stromal protein signatures are significantly different between hormone receptor positive (luminal-like) and hormone receptor negative (basal-like) tumors, being prognostically independent of intrinsic molecular classification, after external validation. Studies of cell lines (whole cell lysates and secretomes) have indicated marked differences between subtypes (luminal-like and basal-like), both baseline and after exposure to hypoxia, indicating subtype-specific metabolic responses, and differential activation of tumor-based stimulation of the microenvironment, such as angiogenesis (manuscript in prep).

Transcriptomics data, supplemented by protein expression information, indicate that the tumor microenvironment in breast cancer is very different between molecular subtypes, and that angiogenic, immunogenic, and neurogenic responses appear to be coordinated. These phenotypes differ according to basic tumor characteristics and disease progression and might provide novel biomarkers and targets for more precise patient management (manuscript in prep).

Expression status of Nestin (mRNA and protein), a candidate biomarker for aggressive breast cancer, was found to correlate strongly with basal-like and BRCA1-associated tumors (Krüger et al, 2017), and also associated with stemness and angiogenic profiles. Cell line studies, using CRISPR technology, are ongoing to map the proteome units and signaling pathways influenced by Nestin.

Current challenges in the field
A major challenge in the field of tissue profiling is to account fully for the complexity and heterogeneity within malignant tumors. Future studies will have to improve information on spatial resolution of molecular data represented from tissue studies, using different end-points such as cancer diagnostics, prognostic profiles, and in particular predictive signals as integrated parts of precision oncomedicine. Ultimately, complex biomarker profiles should translate into improved biological understanding and better diagnostics and treatment.

CCBIO focus in the coming years
Projects will explore the phenotypic diversity in breast cancer, with special focus on tumor-microenvironment characteristics and classification. Cancer tissue and cell line proteomics will be complemented by advanced profiling using the recently established imaging mass cytometry (IMC) platform at CCBIO. ••

GROUP MEMBERS:

Senior researchers:
Akslen, Lars A., MD, PhD, professor, group leader
Arnes, Jarle B., MD, PhD, senior consultant
Aziz, Sura, MD, PhD, senior researcher
Bachmann, Ingeborg M., MD, PhD, professor
Halvorsen, Ole Johan, MD, PhD, professor
Hugdahl, Emilia, MD, PhD, researcher
Klingen, Tor Audun, MD, PhD, researcher
Knutsvik, Gøril, MD, PhD, researcher
Ladstein, Rita Grude, MD, PhD, associate professor
Ramnefjell, Maria, MD, PhD, researcher
Stefansson, Ingunn M., MD, PhD, professor
Wik, Elisabeth, MD, PhD, associate professor

Postdoctoral fellows:
Birkeland, Even, PhD
Edelmann, Reidun, MD, PhD
Finne, Kenneth, PhD
Schuster, Cornelia, MD, PhD
Dimitrakopulou, Konstantina, PhD

PhD candidates:
Askeland, Cecilie, MD
Børretzen, Astrid, MD
Chen, Ying, MD
Kjølle, Silje, Msc
Pilskog, Martin, MD
Smeland, Hilde Ytre-Hauge, MD

Pre-PhD projects:
Litlabø, Hanne Bjelland
Svanøe, Amalie
Sæle, Anna, MD

Technicians:
Hallseth, Gerd Lillian, senior engineer
Kalvenes, May Britt, PhD, senior engineer
Winge, Ingeborg, PhD, senior engineer
Ardawatia, Vandana, PhD, senior engineer

JAMES B. LORENS

Research focus
The group aims to understand the molecular mechanisms that underlie acquired cancer drug resistance. Ultimately, the goal is to improve the ability to prevent and treat cancer drug resistance by elucidating how tumor cells activate cellular plasticity reprogramming within the tumor microenvironment.

Projects
• AXL as a novel regulator of phenotypic plasticity in normal epithelial stem cells.

• Molecular mechanisms of acquired drug resistance to targeted cancer therapies.

• The role of AXL at the tumor-immune interface.

• Improving immunotherapy by AXL inhibition.

• High dimensional analysis of tumor-immune dynamics in the tumor microenvironment.

Important results
• Studies have determined that the AXL receptor tyrosine kinase is a key mediator of acquired therapeutic resistance to different classes of anti-cancer agents, including chemo-, targeted- and immune-therapeutics. AXL is associated with tumor phenotypic plasticity reprogramming that engenders enhanced cell survival attributes.

• AXL is a key component of the immunosuppressive tumor microenvironment. AXL targeting in murine carcinoma models simultaneously reverses tumor epithelial plasticity, and repolarizes suppressive tumor associated macrophages leading to improved responses to chemotherapy.

• AXL targeting in combination with immune checkpoint blockade affects tumor-myeloid cell crosstalk in the tumor microenvironment, leading to improved treatment efficacy.

• AXL is a novel regulator of mammary epithelial stem cell activity, revealed by murine genetic models and high dimensional mass cytometry analysis of normal human breast epithelia.

• Microenvironmental microarray technology (MEMA) showed that AXL-mediated plasticity reprogramming is activated by specific ECM and cytokine components of the tumor microenvironment, and drives acquired drug resistance.

Current challenges in the field
In spite of the significant advances in new anti-cancer treatments, notably immunotherapy, most patients still do not achieve long-lasting clinical benefit. Tumor cell plasticity reprogramming has emerged as a critical driver of acquired resistance and therapeutic failure in patients. Improved methods to detect and target these mechanisms are essential to improve patient outcomes.

CCBIO focus in the coming years
The group will continue to decipher the unique signaling and reprogramming role of AXL in tumors. They will apply high dimensional single cell technologies to build better understanding of how tumor cells exploit AXL at the tumor-immune interface, and use this knowledge to develop unique biomarkers for improved treatment. ••

GROUP MEMBERS:

Lorens, James, MS, PhD, professor, group leader
Berge, Sissel Vik, chief engineer
Bougnaud, Sebastien, PhD, researcher
Chen, Ying Yi, researcher
Davidsen, Kjersti, MD, PhD candidate
Dhakal, Sushil, MS, PhD candidate
D'Mello, Stacey, PhD, researcher
Engelsen, Agnete, MS, PhD, researcher
Ertsås, Henriette Christie, MS, PhD candidate
Kang, Jing, MD, PhD candidate
Lotsberg, Maria Lie, MS, PhD candidate
Madeleine, Noëlly, PhD, postdoc
Stigen, Endre, staff engineer

DANIELA COSTEA

Research focus
The goal is to understand the role of epithelial-mesenchymal interactions in carcinoma progression and development of nano-based vehicles for its targeting.

Projects
• Epithelial-mesenchymal interactions in oral squamous cell carcinoma. The focus is on understanding the mechanisms of metabolic reprogramming of carcinoma associated fibroblasts, their role for the increased glycolytic metabolism of oral squamous cell carcinoma, and the correlation between genetic alterations in tumor cells and activation of fibroblasts.

• Establishing reliable experimental models for vulvar squamous cell carcinoma. These will be further used to investigate differences in energy metabolism and epithelial-mesenchymal interactions between HPV- and HPV+ cancer cells and surrounding fibroblasts. This project is in collaboration with CCBIO Associate Investigator Line Bjørge.

• Exploring the use of an electronic nose device as a screening tool for head and neck cancer. This project is run in collaboration with the Aenose Company and the University of Maastricht, Netherlands, and the University of Khartoum, Sudan.

• Development of functionalized nano-diamond particles for targeting carcinoma associated fibroblasts.

Important results
• Carcinoma cells and surrounding fibroblasts become metabolically coupled through several processes. Cancer associated fibroblasts were found to export mitochondria towards carcinoma cells through both direct contact and via indirect mechanisms in addition to changing their metabolic phenotype when co-cultivated with cancer cells, by undergoing aerobic glycolysis, hypoxia and mitophagy.

• The group developed and characterized a novel and unique vulva carcinoma cell line from a patient with lichen sclerosus. Together with normal and carcinoma associated vulva fibroblasts, this was used to generate robust 3D *in vitro* models and *in vivo* xenografts modeling vulva squamous cell carcinoma occurring in lichen sclerosus patients. This model is currently used to further explore the epithelial-mesenchymal interactions in this type of cancer.

• A specific breath volatile organic compounds pattern for HNC Sudanese patients has been first developed in the hospital settings of Sudan. Analysis of data collected from 160 patients and controls using this specific pattern, shows that eNose testing reaches the specificity and sensitivity levels required for use as a screening tool.

• Functionalized nano-diamond particles for targeting both carcinoma cells and carcinoma associated fibroblasts have been synthesized and are in the *in vitro* testing phase.

Current challenges in the field
Despite an increasing amount of novel pharmaceuticals, cancer therapeutics has currently the lowest clinical trial success rate of all major diseases. This is at least in part due to inadequate pre-clinical models that are limited in modeling human cancer pathways in a realistic biological context, and the paucity of more coordinated efforts from multiple fields. Therefore, the group directs its efforts to establish human *in vitro* 3D models for squamous cell carcinoma and is using them for testing new methods for targeting epithelial-mesenchymal interactions and for impairing tumor progression, together with collaborators from diverse fields such as organic chemistry, tissue engineering and clinical oncology.

CCBIO focus in the coming years
The group will continue to direct its efforts towards better molecular understanding of epithelial-mesenchymal interactions, particularly the metabolic coupling and its targeting using novel nano-based vehicles to impair tumor progression. ••

GROUP MEMBERS:

Senior researchers:
Costea, Daniela Elena, DDS, PhD, professor, group leader
Johannessen, Anne Christine, MD, DDS, PhD, professor
Liang, Xiao, DDS, PhD, researcher
Neppelberg, Evelyn, DDS, PhD, associate professor
Nginamau, Elisbeth Sivy, MD, PhD, researcher

Postdoctoral fellows:
Suliman, Salwa, DDS, PhD

PhD candidates:
Ahmed, Israa, DDS
Das, Ridhima, DDS
Dongre, Harsh, MS
Guerreiro, Eduarda, MS
Mohamed, Hassan Abdel Raouf-Ali, DDS
Mohamed, Nazar, DDS
Mohamed, Nuha, DDS
Dhakal, Sushma Pandey, DDS
Rajthala, Saroj, MS
Xenaki, Victoria, DDS

Pre-PhD projects:
Golburean, Olga, master student
Garujel, Rashmi Chetri, DDS, master student
Rolland Jacobsen, Martha, dental student

Guest researchers:
Litlekalsøy, Jorunn, MS, PhD
Manrikyan Gayane, DDS
Papian, Andrew, MD
Zhuoyuan, Zhang, DDS

Technicians:
Fromreide, Siren
Kalvenes, May Britt, PhD

CAMILLA KRAKSTAD

Research focus
The main research goal of the Gynecologic Cancer Research Group is to identify molecular alterations underlying initiation and development of gynecologic cancers and to translate this knowledge into clinical robust biomarkers.

Projects
• 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 is performed in close collaboration with Professor Beroukhim, The Broad Institute, USA (CCBIO affiliated).

• Comprehensive profiling of genetic alterations linked to molecular subtypes of cervical cancer is ongoing in collaboration with Professor Ojesina, UAB, USA.

• Molecular biomarkers and genetic data are combined with preoperative imaging parameters derived from PET-CT and/or MRI. This project is in collaboration with Professor Ingfrid Haldorsen and provides exciting information on tumor characteristics and potential new imaging-based preoperative biomarkers.

• There is a lack of good model systems for endometrial cancer. The Gynecologic Cancer Research Group is constantly working to develop better 2D and 3D cell models in parallel with developing relevant mouse models. Both imaging and molecular biomarkers are explored in endometrial cancer orthotopic mouse models.

Important results
The team identified Asparaginase-like protein 1 (ASRGL1) as an independent prognostic biomarker in endometrial carcinoma and found that expression of ASRGL1 is lost in metastatic lesions. Also, using specimens from the multicenter study MOMATEC1, the group found that ASRGL1 expression in curettage specimens independently predicts lymph node metastasis in endometrial carcinoma. They identified PIK3CA amplification to be associated with aggressive disease, suggesting that PIK3CA amplification might be a surrogate marker for the serous-like somatic copy-number alteration–high subgroup of endometrial cancer. Continuous work to improve mouse models for endometrial cancers also resulted in development of a new orthotopic model with controllable estrogen exposure. This is an excellent *in vivo* tool to further explore endocrine drug regimens and novel endocrine drug targets for EC.

The MOMATEC2 study is ongoing and the international inclusion of patients has been well established. An interim analysis has been performed for the Momatec2 study, and a report has been prepared and will be circulated to participating centers in 2019. To further explore aspects of hormone regulation in EC, the group investigated the relation between blood steroids and aggressive disease. Several plasma steroids were established as promising biomarkers. The association between increased estradiol levels and a high percentage of visceral fat indicates a larger contributor to estradiol production compared to subcutaneous fat in this population.

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.

CCBIO focus in the coming years
The group commends CCBIO's large network that allows close collaborations between research groups with similar focus but different expertise, and will use this to continue developing their collaboration with groups in the CCBIO family. They also aim at establishing new collaborations with CCBIO's associated international investigators. They will continue to use the CCBIO research school to train their PhD candidates and the regular seminars and annual symposium to interact and develop collaborations and future projects. ••

GROUP MEMBERS:

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

Clinical staff:
Enge, Elisabeth, study nurse
Pridesis, Ann-Helen, study nurse
Valen, Ellen, study nurse

Postdoctoral fellows and researchers:
Espedal, Heidi, MSc, PhD
Halle, Mari Kyllesø, MS, PhD
Høivik, Erling, MS, PhD
Jacob, Havjin, MSc, PhD
Strand, Elin, MSc, PhD
Tangen, Ingvild Løberg, MPharm, PhD

PhD candidates:
Berg, Hege Fredriksen, MSc
Dybvik, Julie, MD
Eldevik, Kristine Fasmer, MSc
Engerud, Hilde, MD
Fonnes, Tina, MedVET
Forsse, David, MD
Lura, Njål, MD
Ytre-Hauge, Sigmund, MD
Åse, Hildegunn, MD

Technical support:
Edvardsen, Britt
Madissoo, Kadri

Medical student:
Myrvold, Madeleine

Master student:
Sødal, Marte

ELISABETH WIK

Research focus
The main research interest is tissue biomarkers in breast cancer, with a particular focus on breast cancer of the young. The aim is to translate integrated multi-level tissue data into more precise diagnostic and therapeutic approaches, for improved survival and quality of life. Dr. Wik works in close collaboration with Professor Lars A. Akslen on breast cancer biomarker studies, and she is the leading investigator for studies focusing on young breast cancer patients. Wik is experienced in integrating large-scale omics data and clinico-pathologic information, and focuses in particular on age-related biologic characteristics in breast cancer and its relation to the established molecular subtypes. Dr. Wik was recruited to a permanent faculty position (associated professor) in 2018.

Projects
• Microenvironment alterations in relation to angiogenesis in breast cancer.

• Effects of dopaminergic compounds in breast cancer, assessing the potential for drug repurposing in subsets of breast cancer patients.

• Exploring and validating composite (signature) biomarkers, with improved potential for capturing tumor complexity.

• Characterization of tumors of young breast cancer patients, including assessment of the PAM50 signature.

• Estrogen receptor signaling-related biomarkers, including coordinated hormone receptor-immune response programs.

Important results
• Wrap-up phase of several postdoc papers (topics: neuro-angiogenesis; angio-immunogenic properties in subsets of breast cancer).

• Recruitment of one PhD student and two Medical Research Program students that will start in 2019.

•First (core) paper on the cohort of young breast cancer patients to be published in 2019.

• As coordinator of CCBIO's INTPART project, several collaborative activities between CCBIO and the Vascular Biology Program (VBP) at Boston Children's Hospital and Harvard Medical School were successfully initiated, e.g. CCBIO907 Cancer Related Vascular Biology (a 3 week course), a lab visiting exchange program and a seminar in scientific writing (2-day course).

Current challenges in the field
Taking tumor complexity and heterogeneity into account in tissue based studies of cancer biomarkers is a true challenge that needs focused attention. Further, strengthening the integration of multi-level omics data in biologically meaningful ways in translational biomarker studies is needed, along with translation of the 'result-omics' into biological and clinical relevant information.

CCBIO focus in the coming years
Imaging mass cytometry (IMC) technology will be applied on FFPE breast cancer tissues from different cohorts, for example in the project on ER-related biology and immune responses (Anna Sæle). Multi-level computational diagnostics in breast cancer will be explored, and a prospective breast cancer biobank will be established. As a recently appointed associate professor at UiB, one major goal is to establish research and educational collaborations within and outside of the CCBIO local, national and international networks.

An important and continued aim is to collaborate with the CCBIO ELSA/RRI team, and include aspects from studies of the humanities in the group's projects.

Dr. Wik is the director of the CCBIO Research School for Cancer Studies, and plans to consolidate the existing program and further develop research school activities. ••

GROUP MEMBERS:

Wik, Elisabeth, MD, PhD, associate professor, group leader
Svanøe, Amalie, medical student, pre-PhD
Sæle, Anna, medical student, pre-PHD

Team 5

Clinical Applications and Trial Studies

The aim of this program is to perform clinical trials with associated biomarker studies, and to promote novel findings on markers and treatment targets for clinical implementation and change of practice. This team consists of the Principal Investigators Gjertsen (CCBIO co-director) and Straume, and Associate Investigator Bjørge.

BJØRN TORE GJERTSEN

Research focus
The 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 the effect of targeted inhibitors of signaling on cancer cells, host immune cells and stromal cells.

Projects
• Biomarkers in phase Ib/II trial in AML with Axl inhibitor bemcentinib (BGB324). Part A of this trial was completed in 2018, and part B which explores various arms of monotherapy (AML, MDS) or combinations (AML; decitabine or cytarabine) will be completed in 2019. This inhibitor does not target a particular driver mutation, but inhibit Axl receptor tyrosine kinase that represents an intrinsic resistance against such targeted therapy.

• Single cell signaling profiling is shown to predict optimal disease control within one week of first dosing with kinase inhibitor monotherapy in chronic myeloid leukemia (CML). The new project (2018-2021) on development of dual and specific CSF1R/FLT3 inhibitors will build on experience with bemcentinib and kinase inhibitors in CML.

• 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.

• Liquid biopsy monitoring of cancer patients in clinical trials. The group is testing the concept of liquid biopsy from sample collection via analysis platforms (e.g., NGS panels and digital droplet PCR) to bioinformatic analyses and interpretation in relapse situations.

Important results
A wide phosphoprotein screen in AML patient cells has recenty been presented (Forthun et al., 2018). Next generation proteomics methodology is now used on patient material from leukemia patients treated with bemcentinib or intensive chemotherapy.

Careful examination of p53 isoforms in serous endometrial carcinoma indicate that the p53 isoform γ is associated with reduced progression-free survival (Bischof et al., 2018). Isoform analyses in ovary cancer are prepared for publication. This may suggest a new target in therapy of these aggressive TP53 mutated cancers.
Analyses of cell free DNA in plasma have indicated the power of various techniques of DNA detection in serum from trial patients. The focus is now on the follow up study with bemcentinib in combination with pembrolizumab or dabrafenib/trametinib in metastatic melanoma (ClinicalTrials.gov Identifier: NCT02872259).

Current challenges in the field
Clonal selection during cancer therapy is likely the most important challenge in therapy of acute myeloid leukemia. Furthermore, the stromal effects and the immunomodulation provided by targeted small molecule kinase inhibitors are not fully understood, and methodologically there is still no technique in clinical diagnostics that can provide such information.

CCBIO focus in the coming years
A CCBIO initiated health trust strategic grant on personalized cancer therapy and liquid biopsy (Helse Vest) will be completed in 2019. The team is working toward publication of analyses based on the mass cytometry platform, detecting rare cells like circulating tumor cells and endothelial progenitor cells, as well as cell free tumor DNA in cancer patients.

Of pivotal importance in 2019 will be to examine single cell analysis of bemcentinib treated AML. The project has synergies with the CSF1R/FLT3 project, developing novel kinase inhibitors against stromal and tumor-host mechanisms. The imaging mass cytometry tissue platform is an important tool that will be fully implemented during 2019 for analyses of patient samples and pre-clinical models. ••

GROUP MEMBERS:

Researchers:
Gjertsen, Bjørn Tore, MD, PhD, professor, group leader
Andresen, Vibeke, MSc, PhD, senior researcher
Brodal, Hans Petter, MSc
Forthun, Rakel Brendsdal, MSc, PhD
Gavasso, Sonia, MSc, PhD
Hovland, Randi, MSc, PhD, senior researcher

Postdoctoral fellows:
Hellesøy, Monica, MSc, PhD
Jebsen, Nina Louise, MD, PhD
Rane, Lalit Shirish, MSc, PhD
Skavland, Jørn, MSc, PhD
Vestrheim, Liv Cecilie, MD, PhD

PhD candidates:
Bentsen, Pål Tore, MD
Dowling, Tara, MSc
Engen, Caroline Benedicte, MD
Gullaksen, Stein-Erik, MSc
Ha, Trung Quang, MD, MSc
Hajjar, Ehsan, MSc
Leitch, Calum, MSc
Shafiee, Sahba, MS
Sletta, Kristine MSc

MD/PhD projects:
Fagerholt, Oda Helen Eck
Tislevoll, Benedicte Sjo

Technicians:
Bedringaas, Siv Lise, MSc
Høysæter, Trude
Kopperud, Reidun, MS, PhD
Sabir, Misbah, MSc
Wangen, Rebecca, MSc

Master Student:
Motzfeldt, Inga Kristine Flaaten, BSc

Administrative support:
Hjelle, Sigrun Margrethe, MSc, PhD

Apprentice, laboratory technician:
Nguyen, Rebecca

ODDBJØRN STRAUME

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 randomized 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; the main objective is to analyze safety and efficacy of BGB324 (bemcentinib) 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. 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 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 combined with immune checkpoint inhibitors are encouraging.

Important results
Selected results from the projects above:

• 38 patients have received treatment in this national trial. Five regional centers have ongoing inclusion of patients.

• 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.

• The group has found that elevated baseline IL6 in plasma predicts poor response in renal cell carcinoma patients treated with sunitinib.

• The group has examined surgical complications occurring after breast reconstructions in breast cancer patients and shows a significant change in recurrence dynamics in patients that experience complications.

Current challenges in the field.
First, the lack of reliable and robust predictive biomarkers of response to treatment for cancer is a major challenge. Second, in most cancer types, the response to immune checkpoint inhibitors is poor. The group feels the need to develop new strategies to increase response rates in these cancer types. Third, cancer is a systemic disease, and the majority of cancer deaths are due to metastatic lesions. There is a need to increase our understanding on why micrometastatic foci of cancer cells escape from dormancy and cause overt metastatic disease.

CCBIO focus in the coming years
The group will continue collecting data and patient materials (blood/tissue) in clinical trials. They will perform an interim analysis of the ongoing melanoma trial in June 2019, and they are currently in the process of designing a new phase 2 clinical trial in renal cell carcinoma combining cryoimmune therapy with immune checkpoint inhibitors. ••

GROUP MEMBERS:

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

LINE BJØRGE

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

Projects
The following projects are ongoing:
• Female cancer prediction using cervical omics to individualize screening and prevention ([FORECEE], https://forecee.eu).
• Precision medicine in epithelial ovarian cancer – the role of tumor biology for surgical outcomes.

• Image-guided surgery and personalized 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 image-guided surgery (IGS) in ovarian cancer and established a portfolio of different preclinical animal models for ovarian carcinoma. A multiparametric mass cytometry panel for bioprofiling of the tumor microenvironment has been established. The group's very first investigator initiated early-phase clinical study is 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. The study is open and patient recruitment is ongoing. In late 2018, a contract with the pharmaceutical company AstraZeneca was signed for provision of the PARP inhibitor olaparib to be used as the first active treatment arm in the study. Phase I of the group's second investigator-initiated clinical study, INFLUENCE: The influence of cytoreduction on patient-reported outcomes in patients with epithelial ovarian cancer, was initiated during the fall. The recruitment has been good, and the first cohort is already closed.

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, improved value of surgical cytoreduction, and stratified trials. 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 well-being and quality of life is critical.

CCBIO focus in the coming years
The CCBIO platform represents a strong scientific foundation 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 overall goals for the CCBIO work are to establish preclinical tools for individual tumor characterization and to portray the tumor microenvironment and drug responses. The focus will be improvement of existing animal models, standardization of HGSOC-specific immunograms, and establishment of methodology for *in vitro* drug screening. The instruments will be validated through clinical translation into early-phase clinical trials. The final goals are to develop theranostics and diagnostic multiplex assays. ••

GROUP MEMBERS:

Bjørge, Line, MD, PhD, MBA, professor, 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
Augestad, Grete, study nurse
Kleinmanns, Katrin, MSc, early stage researcher, PhD candidate
Dongre, Harsh, MSc, PhD candidate
Thomsen, Liv Cecilie Vestrheim, MD, PhD, postdoc

Team 4

Health Ethics, Prioritization and Economics

The aim of this program is to perform studies on the ethics, economics and priority challenge of the biomarker field, to contribute to improved education of CCBIO scientists in this dimension of the work, and to ultimately influence public debate and policy making in the challenging area of biomarkers and targeted therapy. This team consists of Principal Investigator Strand (middle), as well as Associate Investigators Norheim and Cairns.

ROGER STRAND

Research focus
The group performs 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 the similar ongoing RRI projects (NFR Res Publica and Horizon 2020 Super_MoRRI). They are furthermore developing a joint program 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 a 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 is well on the way to create a joint program with CCBIO ethicists (Norheim, Tranvåg) and economists (Cairns, Seo) 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.

CCBIO focus in the coming years
CCBIO has entered its second 5-year period. Before 2023, the group's challenge is to create a level of ELSA awareness in CCBIO, aiming to make a difference on how cancer biomarker research is and will be performed at the University of Bergen. In this work, they will search for synergy with the Centre for Digital Life Norway, which has a strong RRI profile and of which CCBIO is an associated partner. As for own research, the focus is the integration process with the ethics and economics group into the mentioned joint program.
••

GROUP MEMBERS:

Strand, Roger, MS, PhD, professor, group leader
Bremer, Anne Blanchard, MA, PhD, researcher
Stenmarck, Mille Sofie, medical student
Nilsen, Irmelin W, master student

OLE FRITHJOF NORHEIM

Research focus
The aim of CCBIO is to discover, validate and translate cancer biomarkers. This is part of the personalization of cancer medicine. Norheim's team is interested in how cancer biomarkers can inform health care priority setting. Traditionally, patient groups were characterized by common patterns of their cancer and this was the basis for treatment choices. Now, new sub-groups and even individual patients can be identified by biomarkers, genetic differences and other individual characteristics. On this basis, patients will be treated differently. Some may be offered new and expensive cancer drugs and others will not. This challenges ethical thinking about treating people as equals.

Projects
The team will continue the two projects addressing priority setting challenges in personalized cancer medicine:

• A PhD project investigating how cancer biomarkers inform treatment recommendations for new and expensive cancer drugs. This will be done in two different studies: one survey experiment investigating physicians' preferences when deciding who will be given priority to receive a new cancer drug, and one study examining how new cancer drugs, and especially those involving biomarkers, are evaluated in the Norwegian drug reimbursement system.

• Work together with the ELSA group on two interrelated projects: one theoretical work investigating the ethical challenges emerging when using biomarkers to stratify larger patient groups into smaller and more personalized sub-groups. When is it ethically acceptable to treat patients with the same diagnosis differently? The other project addresses policymakers in an attempt to open a constructive dialogue about how new personalized cancer drugs best can be evaluated, and what implications this has for actual priority setting.

Important results
The first article in the PhD project was published in BMC Cancer in May 2018. In this paper, "Clinical decision making in cancer care: a review of current and future roles of patient age," the role of patient age is examined and provides a basis for future work on subgroups.

Age is associated with, and partly influences, clinical decisions in ways that are both avoidable and unavoidable. In total, these publications show that patient age can be used directly or indirectly – and consciously or unconsciously – to guide decisions.

Deciding when and how patient age can be justified is a question of ethics. In some cases, it is unproblematic. The relation between increasing age and increasing cancer incidence is relevant. Conversely, the poor inclusion of older patients in clinical trials is an ethical challenge. Patient age is often used as a proxy for other individual patient characteristics.

In modern cancer care this practice will increasingly be replaced by biomarkers or composite measures. For other, more value-based relationships between age and decision making, more work is needed: is it ethically justifiable to limit cancer treatment based on patient age? And how will the use of modern biomarkers influence clinical decision making?

Current challenges in the field
The increasing amount of new and expensive cancer drugs entering the market offer opportunities, but also challenges. With often marginal effect and unreasonable pricing, these drugs will impose a heavy burden on the country's publicly financed health care system. There is also an ongoing debate on how these drugs best can be assessed in terms of effect, cost and severity. Last, both of these challenges are even more complicated due to the policy of confidential pricing on all new drugs approved in the reimbursement system.

CCBIO focus in the coming years
The team will continue work on priority setting at both clinical and policy levels. In addition, more theoretical work on the role of cancer biomarkers in priority setting is necessary to answer the pressing ethical question: how to treat people as equals? This stream of work will be conducted in close collaboration with the ELSA group. To continue the good dialogue and exchanges with other CCBIO researchers and clinicians is also a priority. ••

GROUP MEMBERS:

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

JOHN CAIRNS

Research Focus
Health economics in CCBIO has a dual focus on the economic evaluation of cancer biomarkers and on understanding the incentives to combine biomarkers with patented medicines. Health economics is an integral part of the Ethics, Economics and ELSA Research in CCBIO. The Health Economics Group has collaborated successfully in the provision of the course CCBIO903 Cancer Research - Ethical, Economic and Social Aspects and contributed two chapters to Cancer Biomarkers: Ethics, Economics and Society (ed. Blanchard & Strand, 2017).

Projects
The primary health economic projects are the PhDs by Kelly Seo (cost-effectiveness modeling of predictive biomarkers in targeted oncology therapies) and Ana Beatriz Luís (incentives for developing new cancer biomarkers and targeted therapies).

Important results
Ana Beatriz Luís and Kelly Seo have recently collaborated on a paper assessing the impact of cancer biomarkers on health outcomes in Norway. Their results suggest that biomarker tests improve health by ensuring that the right treatment is given to the right patient and that the effect is stronger for cancer types for which fewer drugs are available.

Current challenges in the field
Powerful forces are working to change the nature of the evidence on clinical effectiveness that feeds into priority setting processes, these include: the move towards precision medicine with a consequent fragmentation of markets, the perceived need to speed-up decision making processes giving patients earlier access to medicines, and an increasing emphasis on real world evidence.

CCBIO focus in the coming years
The two health economics PhDs are well-advanced and should be completed over the next year. Plans are currently being developed for a new PhD examining the potential role of observational data in the evaluation of cancer biomarkers to inform priority setting.

It is intended to build on the cost-effectiveness modeling in Seo's thesis by developing economic evaluation of specific cancer biomarkers of central interest to CCBIO. In addition, planning is underway for the next CCBIO903 course to be held December 2019 - January 2020. Finally, a collaborative project on priority setting is planned to exploit the strengths and common interests of the Ethics, Economics and ELSA Research Groups. ••

GROUP MEMBERS:

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

Bioinformatics and Big Data

INGE JONASSEN

Research focus
The Jonassen group is working on development and application of bioinformatics methods contributing to the understanding of tumors and their environments, aiming to aid in selecting appropriate treatments and predict outcome. A focus in earlier years has been on *in silico* deconvolution of expression data. New activity has been initiated towards system medicine approaches targeting leukemia.

Projects
Jonassen is leading a new consortium including also Professor Gjertsen from CCBIO in addition to groups from Germany, the Netherlands and Canada. Funding has been obtained through an ERAPerMed project and Jonassen is currently recruiting a postdoc. The project will include data generation on single cell and bulk samples on genomic, transcriptomic and proteomic levels, systems biology modeling, and machine learning aimed at predicting outcome and aid selection of treatment for individual patients, use of a set of different experimental model systems and pilot clinical trials.

Important results
In 2018, the Jonassen group published a paper together with CCBIO's Professor Akslen and Associate Investigator Wik, describing a novel computational method for deconvolution of expression data. This was published in BMC Bioinformatics and is an important milestone which opens possibilities for new projects and applications utilizing the deconvolution approach to aid in understanding tumor microenvironments and also cell type composition and status in different tumors.

Current challenges in the field
The Jonassen group aims to develop and use mathematical models that capture and predict effects of drugs targeting signaling molecules. Through the new project (above), they have established collaborations with groups having a strong track record in this area. In order to use such models to aid in selecting therapies for individual patients, they aim to utilize machine learning methods. One challenge is the relatively small size of training data that will be available for such approaches. The group's approach will be to summarize the data and model predictions using a small number of parameters enabling learning from smaller training sets. A more technical challenge is the increasing focus from research funding agencies on data management plans and FAIR data sharing. This requires bioinformatics support, but also systematic efforts from those collecting samples and generating data in order to capture and describe in standardized ways meta-data allowing data reuse.

CCBIO focus in the coming years
The new EraPerMed project is tightly linked with CCBIO and will be an important focus for the Jonassen group in the coming three years. In addition they hope to contribute to other on-going efforts within CCBIO and also be active in attracting additional funding to projects relying on computational approaches. ••

GROUP MEMBERS:

Jonassen, Inge, MS, PhD, professor
Dimitrakopoulou, Konstantina, MS, PhD, postdoc
Kjørsvik, Øystein, master student
Musana, Mary Gertrude, master student

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, collaborations, networking, 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 the CCBIO Research School for Cancer Studies to have research based courses on the highest level and to enable co-supervision and exchange of research and postdoctoral fellows.

In 2018, 13 highly ranked international affiliated investigators were employed in this network, and CCBIO has experienced good results in terms of fruitful collaboration and exchange of knowledge.

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 470 peer-reviewed articles in different areas of the life sciences.

Professor Thiery is currently collaborating with Professor Jim 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.

Frédéric Amant

Professor Frédéric Amant, PhD and MD, received his medical degree from the University of Leuven (KU Leuven), Belgium in 1992, completed his specialty training as an obstetrician/gynecologist in 1998, and his subspecialty training in gynecologic oncology in 2000.

Frédéric Amant is currently professor at the KU Leuven, Belgium and University of Amsterdam, the Netherlands. In Amsterdam he heads the department of gynecological oncology of the Netherlands Cancer Institute and the Amsterdam University Medical Centers. 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 founded and 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.

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 Camilla Krakstad from CCBIO, 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. Additionally, progress has been made to incorporate CCBIO groups in the INCIP.

Rameen Beroukhim

Rameen Beroukhim got his PhD at the University of Cambridge in 1996 and his MD at the University of California in 2000. He 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's 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.

Ritva Heljasvaara

Senior Researcher Ritva Heljasvaara received her PhD in 1996 in molecular biology at the University of Oulu, Finland. In 1998 she joined one of the world's leading extracellular matrix (ECM) research groups led by Professor Taina Pihlajaniemi at the University of Oulu, and is currently the co-director of the group. The group formed part of the Finnish Centre of Excellence in Cell-ECM Research of Academy of Finland in 2012-2017, and is now actively participating in efforts to promote the University's research profile in the ECM and fibrosis fields with a specific funding from the Academy for 2017-2021.

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 and translational potential of the ECM components in skin, breast, lung and hematologic malignancies. In 2018 she and her team were awarded the 'Oriontation 100 ideas' prize of the Finnish pharmaceutical company Orion on novel concepts for using ECM as a therapeutic target in solid cancers.

In collaboration with Professor Donald Gullberg, Dr. Heljasvaara is investigating the role of the fibroblast-specific integrin α11 in skin squamous cell carcinoma using the chemical DMBA/TPA-induced mouse 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. In addition to research, Dr. Heljasvaara has contributed to teaching at the Department of Biomedicine in 2018.

Jean-Christophe Bourdon

Dr. Jean-Christophe Bourdon earned his PhD in cellular and molecular biology in 1997 at the Paris XI University, France. He is currently senior lecturer at the School of Medicine at Dundee University. He was co-director of the Inserm- European Associated Laboratory (Toulouse University, France) in 2006-2010 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-supervises a PhD project together with Professor Gjertsen, exploring the roles of the p53 isoforms in the cell plasticity and cell fate decision induced by the new anticancer and anti-metastatic inhibitor of Axl receptor kinase inhibitor developed at CCBIO (BGB324). 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 also like to develop new diagnostic tools related to the p53 isoforms in partnership with CCBIO.

Mark LaBarge

Mark LaBarge studied genetics at the University of California, Davis, and earned his PhD in molecular pharmacology at Stanford University in 2004. He 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 CCBIO PI 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.

Ian Mills

Ian Mills studied biochemistry at the University of Oxford, and went on to earn his PhD in molecular and cellular physiology at the University of Liverpool in 2000. He is currently professor of translational prostate cancer biology at Queen's University of Belfast and John Black Associate Professor of Prostate Cancer at the University of Oxford. In addition he is a visiting scientist at Cambridge Cancer Research UK Institute, an honorary visiting fellow in the Department of Oncology at the University of Cambridge and an affiliate member of the Centre for Molecular Medicine Norway (NCMM).

After three years undertaking a postdoctoral research association in the MRC Laboratory of Molecular Biology in Cambridge, working with membrane curvature and sensing associated with clathrin coated vesicle formation, Professor Mills teamed up with Professor David Neal to establish an uro-oncology research laboratory in Cambridge. In 2010 he moved to Norway as one of the initial group leader recruitments into the newly formed Centre for Molecular Medicine Norway (NCMM) and continued his work on prostate cancer, focusing on the impact of transcriptional and chromatin dysregulation on metabolism and stress response pathways. In 2015, he moved to the Centre for Cancer Research and Cell Biology (CCRCB) at Queen's University of Belfast and worked there on understanding the interplay between these biologies and radiotherapy response, as well as on the development of new pre-clinical models of prostate cancer. In 2018, he became professor of translational prostate cancer biology in Belfast and embarked on establishing a new research team within the Nuffield Department of Surgical Sciences, University of Oxford, having been appointed John Black Associate Professor of Prostate Cancer. In this new role he is working to understand how these biological processes synergize with treatment stress to influence the evolution of prostate cancers, investigating this alongside complementary research teams led by computational biologists, surgical clinician scientists, pathologists and bone biologists. He retains a range of collaborations with groups in Norway, with a number of former group members now establishing independent academic careers there. He hopes to use his affiliation with CCBIO to further catalyze collaborative projects across Norway and between Norway and the UK.

Rolf A. Brekken

Professor Rolf A. Brekken received his BA in biology from Luther College in Decorah, IA and his PhD from UT Southwestern Medical Center. His graduate studies were focused on developing novel therapies that target the vascular compartment of tumors.

Professor Brekken is the Effie Marie Cain Scholar in Angiogenesis Research, vice chair of research in the Department of Surgery, deputy director of the Hamon Center for Therapeutic Oncology Research and chair of the Cancer Biology Graduate Program at UT Southwestern. His laboratory is focused on understanding how the tumor microenvironment affects therapeutic efficacy. Two therapeutic antibodies Professor 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 is focused on three general areas: 1. ECM signaling in tumors; 2. therapeutic immune reactivation; 3. how immune cells contribute to the metastatic cascade.

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 at CCBIO to investigate the microenvironment of pancreatic cancer. Additionally, he has a joint project with Dr. Randolph Watnick at Harvard, which developed through connections made at CCBIO and involves Professors Lars A. Akslen and Jim Lorens.

Randolph Watnick

Dr. Watnick received his PhD in biochemistry and biophysics from Columbia University in 1999, and was a postdoctoral fellow with Dr. Robert Weinberg, Whitehead Institute, Cambridge, MA, until 2003. 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.

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, the Watnick lab has 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.

Klaus Pantel

Professor Pantel did his MD at the University of Cologne in 1986, Dr. Med. at the University of Cologne in 1987 and Dr. Med. Habil. at the Ludwig-Maximillians-Universitaet in 1995. He 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 CANCERID (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 a 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 others 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 was also co-organizer of the CCBIO Satellite Symposium on Liquid Biopsies which took place the day before the CCBIO Annual Symposium, May 22nd 2018 at Solstrand outside of Bergen.

Therese Sørlie

Therese Sørlie got her PhD at the University of Oslo in 2000. She 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 with a particular focus on the cellular origins of breast tumors and further development into the intrinsic molecular breast tumor subtypes. The aim is to identify markers for low risk lesions in the breast that can mitigate overtreatment.

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 DCIS and their impact on risk for progression from DCIS to invasive breast cancer.

Arne Östman

Professor Arne Östman received his PhD in 1990 on platelet-derived growth factor from the Ludwig Institute for Cancer Research, Uppsala University, Sweden. He is currently professor at the Karolinska Institute (KI).

Professor Östman's research is focused on the biology of tumor microenvironment with special focus on tumor associated fibroblasts and their role in cancer progression.

Professor Östman was vice-coordinator of STRATCAN, a government funded initiative for development of excellent cancer research at KI (2010-2018). Since the Professor II appointment at UiB in 2015, Östman has obtained funding from the Norwegian Cancer Society 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. Together with Akslen, Östman acted as co-organizer of the first Scandinavian Pathology Seminar (SCANPATH) at Sotra in 2016, gathering Scandinavian tumor pathologists and cancer researchers. The initiative has since been followed by SCANPATH meetings in Sigtuna, Sweden, in 2017, in Tuusula, Finland in 2018, and it will be held at Os close to Bergen in 2019. Östman also contributed with one chapter to the recent collection of reviews on tumor microenvironment edited by Akslen and Watnick.

Hani Gabra

Professor Hani Gabra took his medical degree at Glasgow University in 1987 and his PhD at Edinburgh University in 1996. After 5 years as clinical scientist and head of the ICRF (CRUK) Ovarian Cancer Cell and Molecular Genetics Laboratory in Edinburgh, Professor Gabra took 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 in 2003. 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 Gynecological 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. As a medical oncologist and scientist, he has made substantial research contributions in the biology of cancer and its therapeutic approaches throughout his career, especially in tumor suppressor biology, the molecular basis of clinical platinum resistance and ovarian cancer multi-omics. He has contributed over 170 peer-reviewed publications, including publications in Nature, Nature Genetics, Nature Reviews Cancer, Cell, Cancer Cell, Lancet, Lancet Oncology and J Clin Oncol, and has been on the editorial board of European Journal of Cancer and Gynecologic Oncology.

In his new role at AstraZeneca, Professor Gabra is involved in new drug development particularly around ovarian cancer and also in novel approaches to translational/clinical trial design. He hopes that there will be many opportunities for collaboration in this new role with CCBIO in gynecological and other cancers.

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 students within the field of cancer research, as well as for students from related research fields. In November 2018, Associate Professor Elisabeth Wik was appointed as the research school leader.

The RSCS is well established as a scientifically stimulating and inclusive meeting place for junior researchers within various areas of cancer and ELSA related research, with a common focus on translational studies of cancer biomarkers. PhD candidates and postdocs have an opportunity to meet each other and discuss 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 interests 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 strategy ensures that the center's younger researchers have access to renowned national and international scientists from other research communities.

In 2018, CCBIO held courses that run continuously, reflecting that they are integral parts of CCBIO's strategic activities, as well as CCBIO903, CCBIO904, CCBIO905 and CCBIO907, a new course on cancer-related vascular biology. The other established courses will be repeated in 2019-2020 when CCBIO's next batch of PhDs and postdocs has been recruited. Also, other RSCS activities are taking place when appropriate.

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 is a highly interactive 5 ECTS credits course. It aims to address issues that cancer researchers and clinicians face every day, such as how to prioritize research questions and how to choose between patient treatments; 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:

- **What are the promises and limitations of the vision of precision cancer medicine?**
- **What is a fair priority-setting for distributing the newest precision cancer therapies?**
- **How can economic models help guide health care resource allocation?**

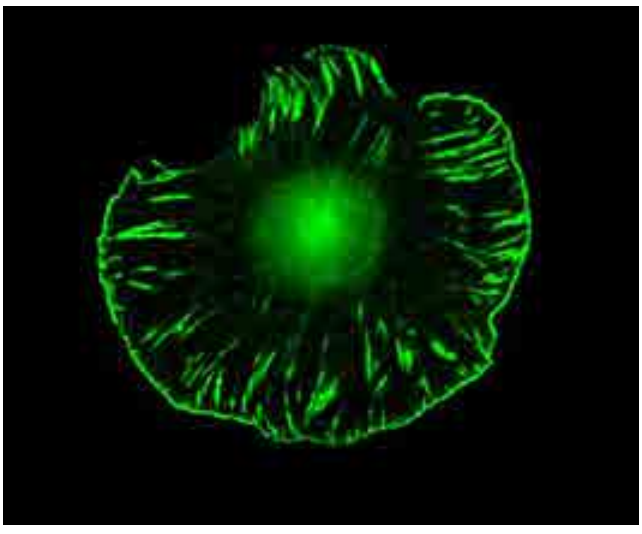
- **Is it at all possible to assess the cost-effectiveness of cancer biomarkers?**
- **How do we make medical decisions when surrounded by risks, uncertainties and even ignorance?**
- **What is a 'good enough' cancer biomarker?**
- **What might a 'good life' be for (future) cancer patients?**

CCBIO903 has been held annually since 2015. In January and February 2018, the course recruited 9 participants and was this time, in addition to the core lectures by the organizers Roger Strand, Anne Blanchard and John Cairns, structured around the edited volume: Cancer Biomarkers: Ethics, Economics and Society. 2017, Eds. A. Blanchard and R. Strand; Norway: Megaloceros Press. The teaching team was extended to some of the co-authors of the book, including Kelly Seo who discussed the limits of assessing the cost-effectiveness of cancer biomarkers; Ole F. Norheim and Eirik Tranvåg who introduced the participants to ethical theories and talked about priority-setting in a context of expensive cancer drugs; Caroline Engen who discussed cancer and the 'good' life, and Elisabeth Wik who had a shared presentation with Anne Blanchard on what is considered as a 'good enough' biomarker in the medical and political settings.

This varied teaching team offered a diversity of perspectives on the ethical, social and economic aspects of cancer research and care, and offered a base for lively discussions and reflections throughout the two weeks. The participants were asked to write a term paper including an analysis of the ethical, economic and social aspects of a topic preferably related to their own PhD project. Based on their ideas for their term paper, the participants also gave an oral presentation in order to receive feedback from the whole group and the lecturers.

CCBIO904 – Biomarkers and Tumor Biology in Clinical Practice

CCBIO904 is a 4 ECTS course covering broad tumor biological topics that are important for understanding how cancer occurs, and the mechanisms that control tumor growth, proliferation and morbidity. The course has particular focus on tumor biological changes and biomarkers that may have or already have significance for personalized cancer treatment and clinical trials studies of new diagnostics and treatment. The course includes lectures, demonstrations, group work, curriculum and a written exam, and aims to give PhD candidates in cancer research a broad understanding of all aspects of tumor biology based on updated knowledge. The PhD candidates also gain deeper insight into how knowledge about tumor biological changes affects our strategies to customize assessment and treatment for this group of patients.



Upon completing this course the candidate should have the skills to:

- **Formulate problems and suggest research on molecular biological aspects in cancer and cancer development in order to map tumor biological mechanisms.**
- **Critically assess the expediency and challenges of using different methods for researching molecular biological aspects of cancer.**
- **Select relevant literature that deals with molecular aspects important in cancer.**
- **Evaluate how knowledge about molecular changes in cancer may provide a better and more precise diagnosis.**
- **Propose new strategies for development of more targeted therapies and testing of cancer drugs.**
- **Understand challenges and possibilities for introducing more targeted therapies and better follow up of cancer patients.**

The candidates need to participate in 90% of the lectures to pass, prepare for and participate actively in the group assignments, and prepare an oral presentation together with the group. The course is completed with a one hour written exam.

CCBIO904 was held for the third time April 23-25 2018. There were 18 participating students from the UiB and other national and international universities/hospitals. Oddbjørn Straume has the academic responsibility and Reidun Kopperud is the course coordinator.

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 as a joint effort with CCBIO RSCS since 2015. BMED904 is a five days course, running every 2 years, and 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.

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

The course was last held in 2017, where 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 next course will be in June, 2019, and will cover various aspects of extracellular matrix (ECM) biology, including the structure and function of the main classes of ECM molecules; 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. John Couchman, Kalle Sipilä and Cathy Merry are confirmed as speakers also in 2019. In addition, Joanna Philips from UCSF will attend and also give a CCBIO Seminar (June 6th) in association with the course. The course is organized and executed by Marion Kusche-Gullberg and Donald Gullberg.

CCBIO905 – Methods in Cancer Biomarker Research

CCBIO905 is a 5 ECTS course geared towards students with an interest in methods relevant for basic and translational cancer biomarker research.

CCBIO905 presents a broad range of topics. In order to cover it all, the 2018 course had 18 thematic parts presented by 16 excellent researchers, including several methods ranging from basic techniques on nucleotides and proteins to more advanced approaches, as well as bioinformatics and biobanking. The lectures were supplemented by a presentation on collaborative clinical studies using biomarkers, held by Professor Bruce Baguley from the University of Auckland, New Zealand. As an integral

part of the course, the students are required to 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 was concluded with a two-hour multiple-choice examination.

The course was established in 2015 and was in 2018 held on August 27-29. In total 30 students were attending the lectures and 15 students attended and passed the exam. Lars A. Akslen and Jim Lorens have the academic responsibility and Ingeborg Winge is the course coordinator.

CCBIO906 – Cancer Genomics

CCBIO906 is a 3 ECTS course providing a 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, and 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 candidates 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 on-line written exam.

CCBIO906 was first held November 1-3, 2017. Eleven participants attended 3 full days with lectures by cancer genomics experts from Bergen and Oslo, followed by group discussions. The next CCBIO906 course is planned for 2020. Ola Myklebost has the academic responsibility, and Solveig Lund Witsø is the course

The aim is to give the candidates 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 on-line written exam.

CCBIO906 was first held November 1-3, 2017. Eleven participants attended 3 full days with lectures by cancer genomics experts from Bergen and Oslo, followed by group discussions. The next CCBIO906 course is planned for 2020. Ola Myklebost has the academic responsibility, and Solveig Lund Witsø is the course coordinator.

CCBIO907 – Cancer-Related Vascular Biology

CCBIO907 is a new 6 ECTS long course covering topics such as basics of vascular biology, vascular biology related therapeutic approaches, biomarkers in vascular biology – from discovery to clinical application, lymphangiogenesis and vascular biology in non-cancerous diseases. Students attending this course will benefit from the knowledge of researchers who have been in the frontline of vascular biology research for decades, and who are experienced lecturers at Harvard Medical School.

Each course week is composed of lectures, group discussions with the international faculty, assignments and presentations, as well as time for self-studies. The course is approved as a PhD course. In the weekly assignments, the students presented project ideas, ranging from hypothesis to suggestions on experimental design including funding proposals.

CCBIO907 is part of the INTPART collaboration between CCBIO and Harvard Medical School and Boston Children's Hospital. In 2018, 15 students attended the full course, while many more seized the opportunity to attend individual lectures and open research seminars.

The first course week, September 17-21, was lectured by Professor Bruce Zetter and Dr. Michael Rogers, both from Harvard Medical School and Boston Children's Hospital. They covered some of the basics of cancer-related vascular biology, along with concepts of cancer biology and precision medicine. Both speakers added experiences and tips to the lectures on how to get key results and achieve progress, as well as building a career. Bruce Zetter also had an additional lecture on how to give a scientific talk. Both lecturers gave open research seminars for a larger audience where they presented up-to-date results from their research on targets for cancer therapies, including stories on drug repurposing and with tips to the audience about recognizing and seizing opportunities for collaborations and idea development. The same week, Bruce Zetter also contributed as speaker at a CCBIO Special Seminar on scientific excellence, along with Merle Jacob (Lund University), Lars A. Akslen and Roger Strand.

The second course week, October 1-5, set out with lectures by local faculty. Reidunn Edelmann guided the students through important details of basic vascular biology, including in-depth lecturing on endothelial biology in inflammation, with highly relevant aspects when aiming to understand vascular biology in cancer. Oddbjørn Straume lectured on anti-angiogenic treatment; about concepts, myths and realities, including clinical examples of effect and lack of effect in anti-angiogenic therapy. The main lecturers this week were Professor Marsha Moses, Director of the Vascular Biology Program at Boston Children's Hospital and Harvard Medical School, and Dr. Roopali Roy, also from the Vascular Biology Program. Professor Moses provided new perspectives and overviews of ways of developing biomarkers, and demonstrated important challenges and possibilities during the steps from biomarker discovery to clinical use. Dr. Roopali Roy gave lectures on proteases and metalloproteinases in vascular biology and cancer, from the basics of this field to current news, also related to results that are relevant for therapy. Professor Moses and Dr. Roy also contributed in an open seminar focusing on mentoring in science, titled "The Importance of Mentoring for Career Development."

The third course week, February 18-22 2019, will cover topics such as lymphangiogenesis, lymphatic metastasis and angiogenesis, also with a focus on ophthalmology. Harvard experts Dr. Diane Bielenberg and Dr. Magali St. Geniez will be teaching. The next CCBIO907 course is planned for the autumn semester 2020. Elisabeth Wik and Lars A. Akslen have the academic responsibility, and Elisabeth Wik is also the coordinator. ••

CCBIO has strong emphasis upon internationalization, as most of the CCBIO groups have a research activity that is inherently international.

International Collaboration and Further Development of Courses

CCBIO has strong emphasis upon internationalization, as most of the CCBIO groups have a research focus that is inherently international. From the start in 2013, CCBIO has aimed to move beyond the usual internationalization measures. As a part of our internationalization effort, we have recruited an international network of adjunct researchers that actively take part in our projects as well as with lectures and tutoring of younger researchers, and during courses and larger meetings. As an example, the CCBIO RSCS will in the early fall of 2019, launch a 2-day thematic course on clinical trials, led by our international adjunct professor Professor Hani Gabra in collaboration with Line Bjørge. Also, a course on innovation is being developed by CCBIO research advisor Yves Aubert.

Developing CCBIO's internationalization effort further, we applied and received funding from the RCN and SIU's program for International Partnerships for Excellent Education and Research (INTPART). INTPART is meant to foster stronger integration between excellent research and excellent teaching in collaboration with international partners. Through CCBIO's INTPART project, we have established a student education and exchange program in collaboration with the Boston Children's Hospital, Harvard Medical School and Harvard Kennedy School.

We would like to list the following examples of outcomes:

- A very successful two-day seminar in scientific writing in December 2017. The seminar is now integrated as an activity of the CCBIO Research School for Cancer Studies (RSCS) program, and will be repeated May 15th and 16th 2019.
- CCBIO907, a course in Cancer-Related Vascular Biology
- Inclusion also of master level students in all CCBIO RSCS courses.
- A lab visit program between CCBIO and the Vascular Biology. Program at Boston Children's Hospital and Harvard Medical School, was established in 2018. Two Medical Research Program students, Amalie A. Svanøe and Martha R. Jakobsen, and one PhD candidate, Silje Kjølle, participated (visit period 4-8 weeks). The students reported great educational and scientific benefit from their Boston stay. The visiting program will be repeated in 2019.
- 1.5 million NOK in funding from the Olav Thon Foundation for student active research in medicine and/or natural sciences/mathematics. This gives our master-level students resources they would otherwise not have access to, further increasing the quality of their training. This funding is fully integrated into the INTPART project.
- The ELSA-team has established INTPART collaborations with the STS program 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.
- A scientific summer school is planned at Iceland. There will be joint participation from faculty and students from both CCBIO and the US-based partners. Iceland is ideally placed as it is the geographic middle point between Boston and Bergen.

CCBIO's INTPART project is coordinated by Elisabeth Wik and Randy Watnick. Watnick is an adjunct researcher in CCBIO's international network and associate professor at the Vascular Biology Program, Harvard Medical School, and coordinates the Harvard part of the project. ••

Researcher Training

The centrally organized part of CCBIO's researcher training is the CCBIO Research School for Cancer Studies (RSCS), coordinated by Associate Investigator Elisabeth Wik. The RSCS is a scientifically stimulating and inclusive meeting place for junior researchers within various areas of cancer research, and has a common focus on translational studies of cancer biomarkers. It also serves as a bridge to CCBIO's ELSA efforts. PhD candidates and postdocs meet each other and deliberate upon their research projects across the established groups. CCBIO stimulates postdocs to increasing independence and encourages the experienced postdocs to provide guidance to younger researchers within the different CCBIO research groups.

Throughout 2018, CCBIO had a total of 58 PhD students, of which 65 % were female. Roughly half were of Norwegian origin and among the remainder, Africa and Asia were particularly well represented with about a third of all PhDs.

Doctoral Defenses

In 2018, 9 of the students affiliated to CCBIO graduated, their work ranging from basic to translational and clinical studies.

TOR AUDUN KLINGEN:
"Vascular invasion by tumor cells, and other prognostic factors in a population-based breast cancer study." Supervisors: Professor Lars A. Akslen and Associate Professor Elisabeth Wik.

STEIN-ERIK GULLAKSEN:
"Single cell signaling and immune profiles in chronic myeloid leukaemia." Supervisors: Professor Bjørn Tore Gjertsen, and Associate Professor Jorunn Kirkeleit and Professor Emmet McCormack.

HENRIETTE CHRISTIE ERTSÅS:
"The effects of ageing on microenvironment-contextual epithelial cell signaling." Supervisors: Professor James B. Lorens and Professor Rein Aasland.

MARIA PAULA RAMNEFJELL: "Prognostic biomarkers and clinico-pathologic characteristics in non-small cell lung cancer. A study with special focus on tumor-vascular interactions." Supervisors: Professor Lars A. Akslen and Associate Professor Lars Helgeland.

WAQAS AZEEM: "Regulatory patterns in prostate cell differentiation – investigation of transcription factors AR, GATA2 and NKX3-1." Supervisors: Professor Karl-Henning Kalland and Professor Xisong Ke.

LAWRENCE FRED SEMBAJWE: "EXT Proteins: Role in Heparan Sulfate Assembly and in Tumor Biology." Supervisors: Professor Marion Kusche-Gullberg, Professor Donald Gullberg and Professor Helge Wiig.

EMILIA HUGDAHL: "Prognostic and molecular markers in primary and metastatic cutaneous melanoma." Supervisors: Professor Lars A. Akslen and Associate Professor Rita Grude Ladstein.

ISRAA ABDULRHMAN AHMED: "Identification of prognostic biomarkers for oral squamous cell carcinoma. Study on human samples and experimental models." Supervisors: Professor Daniela Elena Costea, Professor Anne Christine Johannessen and Associate Professor Dipak Sapkota.

TINA FONNES: "Preclinical models and molecular biomarkers – tools to improve treatment in endometrial carcinoma." Supervisors: Professor Camilla Krakstad, Professor Emmet McCormack and Professor Bjørn Tore Gjertsen.

Bioinformatics Group

The CCBIO Bioinformatics Group (BIG) has been running for 4 years, with the aim to facilitate work on bioinformatics analyses and big data processing, and to increase cooperation in these matters across CCBIO's research groups. Elisabeth Wik is the BIG coordinator. Kjell Petersen and Charitra Kumar Mishra in the BIG support group represent the technology platform ELIXIR which is coordinated by the Computional Biology Unit at UiB (CBU is directed by Inge Jonassen), offering open monthly workshops on bioinformatics and handling of big data.

In 2018, Petersen and Wik contributed to the CCBIO Research School course CCBIO905 Methods in Cancer Biomarker Research, with joint lectures on bioinformatics and translational applications of such analytic approaches. As BIG activities are running according to need and wishes amongst the CCBIO researchers, 2018 was a year without other specific, scheduled activities. The Hyperion imaging mass cytometry (IMC) is currently being established at CCBIO, and will be a used by several of the CCBIO research groups, generating very large amounts of data. Due to this, the BIG activity in coming years is expected to increase significantly ••

Junior Scientist Symposium

The CCBIO Junior Scientist Symposium (JUSS), which also constitute the PhD course CCBIO901, aims to let junior scientists organize and present their research in an environment of peers, and give them the opportunity to get feedback across disciplines. The setting is friendly and acts as a practising arena for the participants to ask relevant questions to presenters and joining academic discussions. Participants will be able to exchange technical expertise, experience and practice with the aim of improving the scientific quality for all.

Throughout the seminar series, researchers early in their career will be introduced to tools and transferable skills they may need to further their career, such as presentation skills to use in front of an audience and in writing, as well as media handling and evaluation of ethical aspects of their daily work. Students signed up for the CCBIO901 will get 3 ECTS, provided that they actively participate in minimum 4 symposia, write a 3 pages long scientific report from 4 elective presentations, and give an oral presentation based on his/her own method(s) at one of these symposia. Other students, staff and visitors are also welcome to the Junior Scientist Symposia.

During 2018, three half-day symposia and one special lunch-to-lunch symposium were arranged with approximately 35 participants at each seminar. The programs included presentations from PhD candidates, postdoctoral fellows and other researchers as well as inspirational lectures by senior researchers such as Anne Christine Johannessen and Bruce Baguley. The inspirational lectures provided insight into how successful research careers can develop, with the aim to inspire early career participants to make their own research path.

The last symposium of 2018 was arranged at Panorama Hotel & Resort, Sotra, and was held in a "lunch to lunch" format, starting with an ice-breaking lunch for participants and presenters before the scientific program commenced. Feedback on this symposium was excellent. The participants enjoyed the two workshops, "How to present your work in 3 minutes" (Marion Solheim) and "How to make great figures" (Michaël Marie), and were inspired by Stein Ove Døskeland, Roland Jonsson and Nils Halberg.

Throughout the year, the high quality presentations by participating PhD students and postdoctoral fellows, the enthusiasm of presenters and audience, and the fruitful discussions during the breaks, have proved the JUSS to be an encouraging and outstanding experience for participants and organizers.

In 2018, JUSS was organized and chaired by Researcher Erling A. Høivik and Postdoc Liv Cecilie Vestrheim Thomsen. In addition, Postdocs Reidun Jetne Edelmann (backup) and Kenneth Finne (replacing Erling A. Høivik as coordinator in 2019) co-chaired one symposium each. ••

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
March 8th 2018
Auditorium 4, BB-building

Symposium Chairs:
Liv Cecilie Vestrheim Thomsen and Erling Høivik.

10.00-10.45 Anne Christine Johannessen: "My life in academia - from local to global"
10.45-11.05 Henriette Aksnes: "N-terminal acetylation of actin by NAA80 impacts cell migration"

11.05-11.20 Coffee break

11.20-11.40 Kimberly J. Hatfield: "Establishment of an Ex Vivo Facility in Bergen"
11.40-12.15 Kristine Fasmer: "Does it matter whether your abdominal fat is stored inside or outside in endometrial cancer?"

12.15-12.45 Lunch break

12.45-13.30 Mari Halle: "Targeting receptor tyrosine kinases in cancer"

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
April 26th 2018
Conference room 109F at the BB-building

Symposium Chairs:
Liv Cecilie Vestrheim Thomsen and Erling Høivik.

10.00-10.50 Monika Kvernenes: "The Arts and Craft of giving a presentation"

10.50-11.10 Coffee break

11.10-11.30 Katharina Bischof: "Preclinical imaging of ovarian cancer models aided by the cell surface marker CD24"

11.30-11.50 Sara Ghaderi: "Prescribed medications in survivors of adult-onset cancer in Norway: A register-based study"

11.50-12.10 Sunniva Sakkestad: "What can mass cytometry teach us about immune responses in volunteers experimentally infected with enterotoxigenic escherichia coli?"

12.10-12.50 Lunch break

12.50-13.10 Ragnhild Haugse: "Secrets of a sonoporated cell"

13.10-13.30 Adrian Drazic: "The unique N-terminal maturation process of actin in humans"

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
September 27th 2018
Conference room 109F

Symposium Chairs:
Liv Cecilie Vestrheim Thomsen and Reidunn Jetne Edelmann.

10.00-10.10 Information about the CCBIO Junior Scientist Seminars and the UiB course program

10.10-11.00 Bruce Baguley: "Life in Science"
– Inspirational lecture with plenary discussion

11.00-11.20 Coffee break

11.20-11.40 Mary Gertrude Musana Lie-Nielsen: "Can automated clustering of CyTOF data discover cell types?"

11.40-12.00 Waqas Azeem: "Transcription factor-mediated reprogram-ming of gene regulation in prostate cells"

12.00-12.20 Havjin Jacob: "miRNA as prognostic markers in colorectal cancer"

12.20-12.50 Lunch break

12.50-13.20 Anne Blanchard: "Policy visions of personalized medicine – perspective from the ELSA group"

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
November 19-20 2018
Panorama Hotel & Resort at Sotra

Symposium Chairs:
Liv Cecilie Vestrheim Thomsen, Erling Høivik and Kenneth Finne.

Day 1, Monday November 19th 2018

10.15 Bus departure from Haukeland Campus

12.00-13.00 Lunch at the hotel

13.00-13.10 Welcome and introduction

13.10-14.00 Inspirational lecture by Professor Roland Jonsson, Vice Dean of Doctoral Education at the Medical Faculty

14.00-14.15 Coffee break

14.15-15.00 Researcher Agnete Engelsen and Professor Camilla Krakstad: "Life in Science: Plan your academic career"

15.00-15.45 Coffee break

15.45-18.00 Workshops: Michaël Marie: "How to create great figures" and Marion Solheim: "How to present your work in 3 minutes"

18.00-18.20 Benedicte Tislevoll: "Single cell detection of early therapy response in acute myeloid leukemia by mass cytometry"

18.20-18.40 Hege Fredriksen Berg: "Establishment of organoids as preclinical model in endometrial cancer"

18.40-19.00 Shamundeeswari Anandan: "Deeper characterisation of the tumor microenvironment in ovarian cancer using single cell mass cytometry by time of flight (CyTOF)"

19.30 Dinner

Day 2, Tuesday November 20th 2018

07.00-08.30 Breakfast

08.30-09.20 Inspirational lecture by Professor Stein Ove Døskeland

09.20-09.40 Coffee break

09.40-10.00 Jahedul Alam: "Characterisation of an ITGA11-Cre mouse strain with Cre recombinase expression restricted to subsets of fibroblasts"

10.00-10.20 Kristine Sletta: "Development of novel combined CSF1R/FLT3-targeted therapy for acute myeloid leukaemia"

10.20-10.40 Kenneth Finne: "Proteomic profiles across breast cancer sub types"

10.40-11.35 Inspirational lecture and scientific presentation by Researcher Nils Halberg

11.35-12.00 Closing remarks

12.00-12.50 Lunch

13.00 Bus returns to Haukeland campus

CCBIO
Research Seminars

The CCBIO seminars are CCBIO's monthly research seminars, gathering CCBIO's staff and a wide range of others with a common interest in cancer biomarkers, for an update on cutting edge research. Most speakers are international and all are of a high international standard. The seminars are open to all and well visited.

The aim of the CCBIO Seminars is to convey relevant biomarker research to the local scientific community, also preparing the ground for future recruitment. In most cases, targeted meetings with the speakers are arranged before or after the lectures so that CCBIO's researchers, in particular the younger ones, get the opportunity to discuss projects and collaboration with high level researchers. Each seminar is followed by an informal pizza get-together, making the CCBIO Seminars an arena for informal interaction that both strengthens cohesion and often leads to fruitful scientific collaborations. The seminars are coordinated by CCBIO PI Donald Gullberg, and form part of the PhD-level course CCBIO902. To the mutual benefit of CCBIO and the Department of Biomedicine, the CCBIO Seminars are also a part of the master level course BMED380, for which Beate Stern is the course coordinator. Information on upcoming speakers and abstracts are posted on CCBIO's web page and circulated by means of round-mails, posters and various newsletters, reaching researchers well beyond CCBIO. This ensures participants on all levels from a wide range of UiB and hospital departments. ••

CCBIO Seminars in 2018

01.02.18 // Helge Wiig, Department of Biomedicine, Faculty of Medicine, University of Bergen, Norway. Title: Lessons from a black box – The extracellular microenvironment and lymphatics in malignant tissue.

22.02.18 // Ole Frithjof Norheim, Department of Global Public Health and Primary Care, and CCBIO, University of Bergen, Norway, and the Department of Global Health and Population, Harvard TH Chan School of Public Health, Boston, USA. Title: Can biomarkers improve priority setting for new, expensive cancer drugs?

22.03.18 // Aaron Meyer, Department of Bioengineering, University of California at Los Angeles (UCLA), USA. Title: Engineering more precise and potent TAM-targeted therapies.

26.04.18 // Ian Mackenzie, Centre for Cell Biology and Cutaneous Research, the Blizard Institute, Queen Mary University of London, UK. Title: Stem cell plasticity in head and neck cancers.

31.05.18 // Aurora Martinez, Department of Biomedicine, Faculty of Medicine, University of Bergen, Norway. Title: Pharmacological chaperoning: a potential treatment for genetic diseases, including some cancer syndromes.

07.06.18 // Arvid Lundervold, Department of Biomedicine, Faculty of Medicine, University of Bergen, Norway. Title: Computational imaging and machine learning in biomedicine.

30.08.18 // Edna Cukierman, Department of Cancer Biology, Fox Chase Cancer Center, Philadelphia, PA, USA. Title: Oncogenic synapses; stromal regulators of pancreatic cancer, metabolic support and innate immunosuppression.

27.09.18 // Staffan Strömblad, Department of Biosciences and Nutrition, Karolinska Institutet, Huddinge, Sweden. Title: Novel cell-matrix adhesion structures.

25.10.18 // Arne Östman, Department of Oncology-Pathology, Karolinska Institutet, Solna, Sweden, and CCBIO. Title: Prognostic and response-predictive potential of tumor-stroma cell subsets.

29.11.18 // Frédéric Amant, Center for Gynecologic Oncology, Netherlands Cancer Institute and Academic Medical Center, Amsterdam, the Netherlands, and CCBIO. Title: Cancer during pregnancy: a multidisciplinary approach in an INCIP research setting.

13.12.18 // Cedric Zeltz, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada. Title: Importance of the tumor microenvironment in non-small cell lung cancer: Examples of stromal proteins as potential therapeutical targets.

CCBIO Special Seminars

When CCBIO members have senior researchers visiting outside of the monthly CCBIO seminars or larger meetings, or the opportunity arises to invite especially interesting scientists, CCBIO encourages them to arrange talks under the umbrella of the CCBIO Special Seminars. The special seminars are integrated into CCBIO's seminar series with its support apparatus and wide announcement. In this way, CCBIO gives its members and the wider audience the chance to get input from and interact with high-level researchers. The special seminars have typically been very well visited with 100 participants or more.

Special Seminar 19.09.18, "What is Scientific Excellence?"

Speakers Bruce Zetter (Harvard Medical School and Boston Children's Hospital), Merle Jacob (Lund University) as well as Lars A. Akslen and Roger Strand discussed different ways to conceptualize and achieve excellence, leaving the audience both inspired and a little thought-provoked. In this special seminar, the ambition was to go deeper into the issue of quality and excellence in science. Apart from scholars from the medical fields, the issue also attracted participants from the other UiB faculties, showing the general relevance of the topic.

The speakers and debate participants had no easy answers for the audience but they did provide ideas about elements of excellence: vision, creativity, novelty, and to go for quality above quantity. The balance between focus and openness to other ideas and people was another topic of the discussion. In his talk, Bruce Zetter also insisted on one necessary condition for excellence that never should be taken for granted but sometimes is: research integrity. All speakers agreed that from the point of view of the practicing researcher, there neither is nor can be one recipe or one singular notion of excellence.

Merle Jacob, a leading researcher on research policies and research funding organizations, provided a sobering perspective on the policy goals behind excellence funding. Painting with a broad brush, she described how research communities have been attracted and flattered by policy talk (and money) of excellence. In this way they have allowed themselves to be governed as hoped for by the funding organizations: They have self-organized into more thematic coordination, producing local critical mass on certain research topics. She claimed that "Paradoxically, what the funding organizations wish for, is already to a large extent achieved by the center proposals themselves."

Still, public spending on excellence is in need of justification in terms of its performance, but evaluation of centres of excellence is notoriously difficult: "Given that these centers were already excellent, excellence can not be a credible outcome," she explained. On the other hand, the funding instruments are not set up to encourage research that really is taking high risk. Indeed, funding decisions are in practice made by reference to past achievements, rewarding researchers who have shown excellence in the past.

In sum, research communities' notions of excellence and policy discourses using the same word both exist in the same universe, and the ambitious researcher needs to know them both. Knowing them also means knowing how they differ. While Lars A. Akslen is in charge of an operation that has to report to the Research Council of Norway by their criteria, he contemplated his role as director of a centre of excellence also in terms of how to organize well the research that actually is taking place: "I watch out for the good seeds, and try to create a great soil," he said.

Special Seminar 20.09.18, Cancer-Related Vascular Biology, organized through the CCBIO/Harvard INTPART partnership

The seminar was part of the CCBIO long course CCBIO907 Cancer-Related Vascular Biology, and open to a larger audience than the course participants. Speakers were Drs. Michael Rogers and Bruce Zetter from Boston Children's Hospital and Harvard Medical School. Michael Rogers' talk was titled "Validation of Anthrax Toxin Receptor 2 (Antxr2/CMG2) as a Target for Small Molecule Antiangiogenic Therapy" and

Bruce Zetter's talk "Drug discovery for treating metastatic cancers." Both lecturers presented up-to-date results from their research on targets for cancer therapies, including interesting stories on drug repurposing and with tips to the audience about recognizing and seizing opportunities for collaborations and idea development – which sometimes occur in unexpected settings.

Special Seminar 03.10.18, "The Importance of Mentoring for Career Development"

Seminar organized through the CCBIO/ Harvard INTPART partnership, where panelists Marsha A. Moses (Director of the Vascular Biology Program at Boston Children's Hospital and Harvard Medical School), Roopali Roy (Harvard Medical School/Boston Children's Hospital), Roland Jonsson (Faculty of Medicine/UiB) and Anne Blanchard (SVT/CCBIO, UiB) discussed mentoring in different forms and settings, and provided useful advice and food for thought for both mentors and mentees. Is mentoring just a matter of respecting national legislation? Who should be involved in mentoring? How can we encourage mentoring practices in a more systematic way, particularly in a context of 'fast' research and short-term contracts?

The panelists provided varied and complementary perspectives on mentoring, stemming from their different cultural and disciplinary background, as well as their different experiences as 'mentors' and 'mentees'. It was made clear that mentoring is a long-term effort that goes beyond the time-limited academic support of 'finishing a task' (e.g., delivering a thesis or getting a paper published). Mentoring also engages in reflections on future career paths (both in and outside of academia), and provides insights on the cultural and institutional norms in different fields, both in terms of how the science is produced, but also at a more structural level (gender issues, hierarchy, administrative matters). It is therefore different to 'supervision' or 'coaching', which are more short-term ways of supporting a colleague.

Professor Moses and Dr. Roy shared different models of mentoring, and emphasized the importance of going beyond the traditional 'one-on-one' model. They argued that 'developmental mentoring', where a network of mentors come into play for the different career aspects of the mentee, was useful and efficient for proving the mentee with regular and varied guidance. In that model, the mentee takes an active part in identifying his/her career goals, and maps and conveys his/her own network of mentors who can help both academically and personally. Both Professor Moses and Dr. Roy, respectively in their capacity as mentor and mentee, voiced the importance of initiative- and risk-taking, long-term commitment, fluid communication, flexibility and openness for having a fruitful and mutually benefiting mentoring relationship.

Despite its central importance for creating a research environment that is balanced, innovative and responsible, mentoring faces important structural limitations. As recalled by Professor Jonsson, Vice Dean of Doctoral Education, in 2009 in Norway, only 18% of PhD candidates ended up in a career within academia (these numbers are higher for the fields of medicine and health, with about 53% of candidates continuing in research and development). Dr. Blanchard also pointed at the strong discrepancy between men and women pursuing a career in academia after a post-doctoral project; with much fewer women going on to positions of assistant, associate, and full professor.

In a context of fast science, characterized by short-term contracts, implementing long-term mentoring relationships is difficult, but it is necessary and steps need to be taken to take mentoring seriously systematically.

In sum, while mentoring is one of the main pillars for creative, balanced and responsible research, it is not yet systematically part of the academic culture. The CCBIO Special Seminar on this topic was a first step towards this vision; it started important discussions and showed that these need to be ongoing for mentoring to be taken seriously. ••

Satellite Symposium on Liquid Biopsy

This year, CCBIO established a new tradition of hosting a satellite symposium in connection with the annual symposium, taking place the day before at the same venue. The topic for the first satellite symposium was *Liquid Biopsy*, and the meeting was co-organized by CCBIO, the Bergen Health Strategic Program of Personalized Cancer Therapy (Liquid Biopsies), and Professor Klaus Pantel, University Klinik Hamburg. Professor Pantel is also an international affiliated investigator at CCBIO.

The Satellite Symposium included updates on circulating tumor cells (CTCs), circulating nucleic acids and microvesicles, with emphasis on practical and clinical applications and the biology of metastasis.

The term "Liquid Biopsy" was introduced in 2010 by Catherine Alix-Panabieres and Klaus Pantel, and today, circulating tumor cells (CTCs) and circulating DNA are still the mostly investigated liquid biopsy biomarkers (PubMed harbors today more than 20,000 reports on CTCs).

In recent years, there has been substantial progress in the assay development and clinical data demonstrating that liquid biopsy assays can contribute to early detection of cancer, monitoring of cancer therapies, identification of therapeutic targets and resistance mechanisms and detection of minimal residual disease in cancer patients.

Liquid biopsy and immunotherapy were the two hottest topics at the 2018 Annual AACR Meeting in Chicago in April. The AACR is globally the largest translational cancer society and the Annual meeting had more than 22,000 participants

this year. Naturally, it was fitting that Liquid Biopsy was highlighted at CCBIO's Solstrand event. This was an excellent meeting with internationally recognized experts. The lectures were very informative and the topics were complementary. Most importantly, the presentations inspired very lively discussions with the 72 participants in the audience.

CCBIO will host a satellite symposium to the annual symposium also in 2019, this time on the topic *Deep Tissue Profiling*, May 12th.••

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
May 22nd 2018

Solstrand Hotel & Bad, Os

12.00-13.00	**Lunch**
13.00-13.05	Welcome by Professor Bjørn Tore Gjertsen, Helse Bergen/CCBIO, Bergen, Norway
13.05-13.45	Liquid Biopsies now and ahead: Professor Klaus Pantel, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
13.50-14.30	Isolation, culture and characterization of CTCs: Professor Catherine Alix-Panabières, University Medical Centre of Montpellier, Montpellier, France
14.35-15.15	Exploring tumor heterogeneity within Circulating Tumor Cells: Dr. Costanza Paoletti, University of Michigan Comprehensive Cancer Center, USA
15.15-15.45	**Break with coffee and refreshments**
15.45-16.25	Exosomes/microvesicles: Professor Guido Jenster, Erasmus MC, Rotterdam, the Netherlands
16.30-17.10	Circulating nucleic acids and proteins: Professor Ulf Landegren, Uppsala University, Sweden
17.15-17.30	Liquid biopsies and clinical projects: Bjørnar Gilje, MD, PhD, Helse Stavanger, Norway
17.35-17.50	Circulating tumor DNA as biomarker in clinical trials: Randi Hovland, PhD, University of Bergen / Helse Bergen, Norway
19.30	**Dinner**

Professor Klaus Pantel and other participants continued their stay at the CCBIO Annual Symposium 2018 starting at the same place the next morning May 23rd and 24th and were available for follow-up discussions.

3rd Scandinavian Tumor Pathology Seminar

The 3rd Scandinavian Tumor Pathology Seminar (SCANPATH), with the sub-heading "The Symphony of Biomarkers," was held in Gustavelund, Tuusula, Finland 30th November to 1st December 2018. The local organizers were Caj Haglund, Olli Carpén, Johanna Arola, Jaana Koski-Alhainen and Tiina Vesterinen.

SCANPATH is an annual network meeting for Scandinavian tumor pathologists and pre-clinical scientists with an interest in the prospects of next generation tissue profiling. The meeting was initiated by CCBIO in 2016 and co-organized by CCBIO in 2017. The aim has been to stimulate tissue-based studies of tumor mechanisms and biomarker mapping. This initiative has been a success and SCANPATH is now a well established annual forum.

During this year's SCANPATH, several exciting topics were covered. From CCBIO, Kenneth Finne, Elisabeth Wik and Reidunn Edelmann presented results from their projects. Around 60 participants were gathered at Gustavelund. The meeting in 2019 will again be organized by CCBIO and held at Solstrand Hotel & Bad at Os close to Bergen in October 2019. ••

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM

Gustavelund, Tuusula, Finland

November 30th 2018

11.30-11.40	Introduction by Caj Haglund and Olli Carpén
11.40-12.00	The landscape of Finnish health research: biobanks, FICAN and FinnGen. Johanna Arola, Helsinki
12.00-12.20	What we have learned from the U-CAN project? Per-Henrik Edqvist, Uppsala
12.20-12.40	Dynamic tumor monitoring and adaptive therapy: The only way forward? Karin Jirström, Lund
12.40-13.20	20 x 2 min poster and exhibition pitching. Tiina Vesterinen, Helsinki
13.20-14.20	**Lunch, exhibition and posters**
14.20-14.40	Breast cancer of the young; more aggressive tumor phenotypes. Elisabeth Wik, Bergen
14.40-15.00	Expression of stromal signature markers associates with worse outcome in patients with breast cancer. Kenneth Finne, Bergen
15.00-15.20	Molecular characterization of pseudomyxoma peritonei. Ari Ristimäki, Helsinki
15.20-15.50	**Coffee break, exhibition and posters**
15.50-16.10	Digital Pathology 2.1. Patrick Micke, Uppsala
16.10-16.30	Deep learning for image-based diagnostics. Nina Linder, Helsinki
16.30-16.50	Deep learning for translational research and pathology - towards complete digital diagnostics. Johan Lundin, Helsinki
16.50-17.20	**Coffee break, exhibition and posters**
17.20-17.40	The secretomic background for the distinct histology of papillary renal cell carcinoma. Martin Johansson, Lund
17.40-18.00	Patient-derived cell lines for personalized treatment and stratification of bladder cancer. Pekka Taimen, Turku
18.00-18.20	High grade serous ovarian cancer - towards targeted treatment. Olli Carpén, Helsinki
19.00-23.00	**Dinner**

DECEMBER 1ST 2018

08.30-08.50	The Human Protein Atlas: Spatial proteomics in health and disease. Cecilia Lindskog Bergström, Uppsala
08.50-09.10	Cancer patient therapy stratification based on PP2A activity. Jukka Westermarck, Turku
09.10-09.30	In situ sequencing based immunoprofiling of human tumors. Carina Strell, Stockholm
09.30-09.50	Molecular markers for brain tumor diagnostics. Kirsi Granberg, Tampere
09.50-10.10	**Coffee break, exhibition and posters**
10.10-10.30	PODXL- and EGFR-mediated signaling in gastrointestinal cancer. Anna Larsson, Lund
10.30-10.50	Dysplasia in serrated polyps. Markus Mäkinen, Oulu
10.50-11.10	The role of oral pathogens in general health and the possible role in oropharyngeal and gastrointestinal cancer. Jaana Hagström, Helsinki
11.10-11.40	**Coffee break, exhibition and posters**
11.40-12.00	Multiplex analysis of tumor stroma. Teijo Pellinen, Helsinki
12.00-12.10	Marker- and localization-defined subsets of CD68 positive cells show specific associations with prognosis in high-grade serous ovarian cancer. Sara Corvigno, Stockholm
12.10-12.20	Notch-signaling-defined vessel subtypes in breast cancer. Reidunn Edelmann, Bergen
12.20-12.40	Myeloid derived suppressor cells in breast cancer patients. Karin Leandersson, Lund
12.40-13.00	Concluding remarks by Caj Haglund and Olli Carpén
13.00-	**Lunch and departure**

The 6th CCBIO Annual Symposium 2018

May 23th and 24th 2018, at Solstrand Hotel & Bad

As in earlier years, the CCBIO Annual Symposium reached its maximum capacity of around 200 participants, and the setting could not have been better, with warm sunshine and beautiful fjord surroundings. The symposium consisted of a combination of talks by invited international speakers and other senior and junior researchers, extended poster sessions where younger researchers presented their work, and ample time for interaction between the participants. The venue of a historic hotel in a seaside location with a fjord view, where most participants stayed the night and sat down together for lovely meals, provided an ideal frame for international networking within the field of cancer research.

This year's topics covered issues such as extracellular matrix, RNA therapy, CAR T-cell technology, breast cancer mouse models, stroma characteristics as biomarkers, stress response signaling, non-genetic heterogeneity and non-linear dynamics of tumors, the role of microenvironment in cancer susceptibility and drug tolerance, candidate cells of origin of human breast cancer, clinical trials perspectives

on developing personalized cancer prevention and therapy strategies, predictive biomarkers in the surgical treatment of epithelial ovarian cancer, regulation of erythropoiesis and optimized treatment of anemia, and communication structures of brain tumor cells.

Professor Thomas F. Meyer from the Max Planck Institute for Infection Biology gave a very interesting account of mutations by bacterial pathogens and the relationship between chronic bacterial infections, inflammation and human cancer. He presented studies which indicate that chronic infection induced by sexually transmitted pathogens, including chlamydia, can cause ovarian cancer and uterine cancer.

The program also gave room for a discussion on what it means to be a just and caring society, when we have limit-

ed resources to meet virtually unlimited health care needs. Cancer biomarker research is tied into a very complex web of medical practice, patients' hopes and expectations, health policy, health economics and an extreme complexity and uncertainty around the biology of cancer, which makes it a terrain prone to invisible rationing. Three different perspectives were presented by Leonard Fleck, Oddbjørn Straume and Eirik Tranvåg, and the discussion with the audience continued for almost an hour after the session was formally closed.

As in previous years, a whole session was dedicated to young researchers presenting their recent findings. There were also poster sessions both days, with altogether 42 posters, 21 presented each day. A poster award committee consisting of the CCBIO affiliated investigators Therese Sørlie (Oslo University Hospital and the University of Oslo), Jean-Christophe Bourdon (Dundee University) and Hani Gabra (AstraZeneca in Cambridge and Imperial College London), selected the best 3 posters, awarding Rakel Brendsdal Forthun, Rosalyn Sayaman and Line Pedersen with a diploma each at the end of the symposium.••

Centre for Cancer Biomarkers

6th CCBIO Symposium 2018

Solstrand, May 23-24, 2018 Bergen -Norway

Norwegian Centre of Excellence
The Research Council of Norway

SCIENTIFIC PROGRAM

Day 1: Wednesday May 23rd 2018

09.00-10.00	**Registration and coffee**
10.00-10.15	Lars A. Akslen (Director of CCBIO): Introduction to the CCBIO Symposium 2018
10.15-11.00	Chair: Randy Watnick Richard Hynes: Extracellular matrix vulnerabilities in cancer
11.00-11.30	Bruce Zetter: RNA therapy in the treatment of cancer
11.30-12.00	Frederick Locke: CAR T-cell technology against cancer
12.00-12.30	Thomas F. Meyer: Do bacterial pathogens provoke distinct mutations in their host?
12.30-14.30	**Lunch and poster session I**
14.30-15.00	Chair: Arne Östman Therese Sørlie: Mouse models for breast cancer progression
15.00-15.30	Carina Strell: Exploring stroma characteristics as mediators of breast DCIS progression and as markers for radiation-response
15.30-16.00	Ian G. Mills: Stress response signaling in prostate cancer
16.00-16.30	**Coffee break**
16.30-17.15	Chair: Roger Strand Leonard Fleck: Just Caring Challenges: Visible Biomarkers and Invisible Rationing
17.15-17.45	Comment I: Oddbjørn Straume Comment II: Eirik Tranvåg
19.30	**Dinner**

Day 2: Thursday May 24th 2018

09.00-09.30	Chair: Rolf Brekken Sui Huang: Non-genetic heterogeneity and Non-linear Dynamics of Tumors: Why Cancer Treatment Can Backfire
09.30-10.00	Mark LaBarge: The role of microenvironment in cancer susceptibility and drug tolerance
10.00-10.30	Ole W. Petersen: On the candidate cells of origin of human breast cancer
10.30-11.00	**Coffee break**
11.00-11.20	Chair: Daniela Elena Costea Fanny A. Vatter: High-dimensional analysis of single human mammary epithelial cells with age
11.20-11.40	Kenneth Finne: Proteomic profiles across breast cancer subtypes
11.40-12.00	Gry S. Haaland: Association of warfarin use with lower overall cancer incidence
12.00-12.20	Liv C. V. Thomsen: Cryoimmunotherapy against cancer – status and outlook
12.20-14.20	**Lunch and poster session II**
14.20-14.50	Chair: Karl-Henning Kalland William N. William Jr.: Developing Personalized Cancer Prevention and Therapy Strategies: a Clinical Trials Perspective
14.50-15.20	Christina Fotopoulou: Predictive biomarkers in the surgical treatment of epithelial ovarian cancer
15.20-15.50	Ursula Klingmueller: From insights into regulation of erythropoiesis towards optimized treatment of anemia
15.50-16.20	Hrvoje Miletic: Microtubes – communication structures of brain tumor cells
16.20-16.30	Bjørn Tore Gjertsen (Co-Director of CCBIO): Closing remarks and poster awards

The 6th Annual Symposium

23th-24h May 2018
at Solstrand Hotel & Bad

Dissemination and Communication

Dissemination and Communication

CCBIO aims to disseminate its findings to the public and continues to do this in a timely and informative way. In addition to publications and events for the scientific audience, our research can be viewed, read and listened to in national mainstream media and at public popular scientific meetings and debates. CCBIO also has a dissemination effort aimed especially at children in collaboration with the actor Henriette Christie Ertsås. She gives performances and lectures on cancer and biomarkers at schools on CCBIO's behalf.

Example of Facebook entry. Visit from the NRK (the Norwegian public national television and radio broadcaster), where the CCBIO director explains about CCBIO's work, and shows "the treasures"; the biobanks in the halls underneath the hospital.

Public debate 22.08.18, "Tomorrow's cancer treatment – for good or bad." Public debate on cancer research and treatment at Litteraturhuset in Bergen which attracted an overfilled auditorium, even having to turn away people at the door. As statistically one third of us will develop some sort of cancer during our lifetime, it is no wonder that this is an issue that attract a large audience. Panel participants were CCBIO Director Lars A. Akslen, cancer patient Astrid Kvale, Regional Manager in the Norwegian Cancer Society Geir Vangsnes and GP and Researcher Knut Arne Wensaas, discussing today's status of cancer treatment, and future expectations. CCBIO Communication's Adviser Marion Solheim was moderator. The debate is available in full (except for questions afterwards), on Youtube.

CCBIO keeps its webpages updated at all times, presenting various news stories from our research community, and ensuring that our numerous open events are well advertized. Also, social media has grown to be a tool and connector for governmental organizations, businesses and individual users. CCBIO promotes our researchers, scientific findings, happenings, media appearances and behind-the-scenes glimpses via the Faculty of Medicine's Facebook, Twitter and Instagram accounts.

CCBIO offers schools a unique way of learning about cancer cells in the form of an entertaining play. Here, cancer cells are introduced in a very amusing and thought-provoking manner. Schools have 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 or stand-up routine "Christine the Cancer Cell - A sociopath in the body," suitable for youth and adults. Both are free of charge. The performer is Henriette Christie Ertsås, PhD graduate from CCBIO at the Department of Biomedicine. Henriette stages stories that take place inside the body, and within the individual cell. She is a molecular biologist who has been working with age-dependent cancer in her PhD project. Having also studied acting, she is well suited to tell the story of the fascinating biology of cells. The plays are supported by CCBIO and the Norwegian Research Council. In 2018, Henriette did altogether 33 plays for schools and adult audiences, receiving enthusiastic acclaim for conveying a complex topic in an easily understandable, interactive and entertaining manner.

From the CCBIO stand at the Research Fair ('Forskningstorget'). Creating an interest in potential young researchers, this year by letting them isolate DNA, palpating tumors in playmice, finding tumors using PET-CT on both mice and patients, as well as looking at cancer cells through a microscope and illustrating a diagnostic mindset. PET-CT and microscopy also engaged the adult audience. For the more creative, there were also opportunities to make pearl bracelets illustrating their own DNA, as well as building a DNA helix.

CCBIO in the Media


Dagbladet

Debatt:

Mammografi er et klokt valg for mange

10.12.18 – DAGBLADET
"Mammografi er et klokt valg for mange" – Lars A. Akslen

25.11.18 – FAGPRESSENYTT
"FAIR data management in molecular life sciences"
– Inge Jonassen


Aftenposten

Debatt

Ja til moderat plan for åpen tilgang til forskningsresultater | 27 forskningsledere

15.11.18 – AFTENPOSTEN
"Ja til moderat plan for åpen tilgang til forskningsresultater
– 27 forskingsledere" – Lars A. Akslen

21.10.18 – DAGENS MEDISIN
"– Bør endre behandlingspraksis for rundt 100 norske kvinner"
– Line Bjørge

21.10.18 – DIGI.NO
"Er i gang med å la maskinene ta over for legene: - Nå jobber vi med de digitale modellene, sier norsk forsker"
– Bjørn Tore Gjertsen


Dagens Medisin

Nyheter Debatt Pharma DM Arena

Skyhøye forventninger til behandling av eggstokkreft

20.10.18 – DAGENS MEDISIN
"Skyhøye forventninger til behandling av eggstokkreft"
– Line Bjørge

24.08.18 – PÅ HØYDEN
"Astrid (31) blir ikkje frisk av kreften – men lever godt med det"
– Lars A. Akslen

23.08.18 – UIB AKTUELT
"Kreftens sporhunder" – Lars A. Akslen

22.08.18 – NRK RADIO
News at 14.30 – interview with Lars A. Akslen

27.06.18 – UIB AKTUELT
"Alle tre gjennom nålauget" – Lars A. Akslen

27.06.18 – PÅ HØYDEN
"Får finansiering for fem nye år" – CCBIO in general


Tidsskriftet

Kreftbiomarkører – et gode eller et onde?

26.06.18 – TIDSSKRIFT FOR DEN NORSKE LEGEFORENING
"Kreftbiomarkører – et gode eller et onde?" – review of the book Cancer Biomarkers: Ethics, Economics and Society by editors Anne Blanchard and Roger Strand

26.06.18 – TIDSSKRIFT FOR DEN NORSKE LEGEFORENING
"Biomarkører og tumors mikromiljø" – review of the book Biomarkers of the Tumor Microenvironment by editors Lars A. Akslen and Randolph S. Watnick

18.06.18 – VG
"Ny forskning: Kan oppdage kreft med blodprøve" – Bjørn Tore Gjertsen


VG

Persontilpasset medisin: Slik skal ny teknologi endre fremtidens kreftbehandling

07.06.18 – VG
"Persontilpasset medisin: Slik skal ny teknologi endre fremtidens kreftbehandling" – Bjørn Tore Gjertsen

06.06.18 – VÅRT LAND
"Ny pille mot aggressiv kreft" – Oddbjørn Straume


abc nyheter / Nyheter Penger Helse og livsstil Motor Reise Stemmer Været

Helse Trening og kosthold Livet Mat og drikke Bolig og interiør Teknologi Tester

Helse

Kreftsvulsten er mer komplisert enn forskere tidligere har trodd

Biw Ellen Jakobsen - Forskning.no

25. juni 2018 16:22 – Oppdatert 25. juni 2018 16:14

Del (164) Tweet Epost

Siden 1800-tallet har medisinere

25.06.18 – ABC NYHETER
"Kreftsvulsten er mer komplisert enn forskerne tidligere har trodd" – Lars A. Akslen

05.06.18 – FIRDA TIDEND
"Norsk firma har utvikla pille mot aggressiv kreft" – Oddbjørn Straume

05.06.18 – ABC NYHETER
"Norsk firma har utviklet pille mot aggressiv kreft"
– Oddbjørn Straume

05.06.18 – BERGENS TIDENDE
"Bergensfirma har utviklet pille mot aggressiv kreft"
– Oddbjørn Straum

04.06.18 – DAGENS MEDISIN
"Her ble det kø" – Oddbjørn Straume

Utvikler pille mot aggressiv kreft: Kan bremse sykdommen for spesielt syke pasienter

CHICAGO (VG) Et norsk firma fra Bergen har utviklet en pille som kan hindre spesielt aggressive kreftformer fra å spre seg.

05.06.18 – VG
"Utvikler pille mot aggressiv kreft: Kan bremse sykdommen for spesielt syke pasienter" – Oddbjørn Straume

Prisdryss til leger

29.05.18 – TIDSSKRIFT FOR DEN NORSKE LEGEFORENING
"Prisdryss til leger" – Ying Chen

26.05.18 – BERGENSAVISEN
"Fysioterapeuten reddet Roars (72) liv" – Ingeborg Bachmann, Rita Ladstein

23.05.18 – DAGENS MEDISIN
"Positive erfaringer med frysing av prostatakreft" – Karl-Henning Kalland

Uheldig hemmelighold

beste helsevesen?

03.05.18 – BERGENS TIDENDE
"Uheldig hemmelighold" – Ole Frithjof Norheim

25.04.18 – SCIENCE NEWSLINE
"Changes in Breast Tissue Increase Cancer Risk for Older Women" – James Lorens, Mark LaBarge, Fanny Pelissier.

24.04.18 – MEDICALXPRESS
"Changes in breast tissue increase cancer risk for older women" – James Lorens, Mark LaBarge, Fanny Pelissier.

20.04.18 – DAGBLADET
"Det lille implantatet skal redde liv: Får du en flekk på huden – kan du ha kreft" – Oddbjørn Straume

19.04.18 – BERGENS TIDENDE
"Lovende resultater for bergensk kreftvaksine"
– Karl-Henning Kalland

03.04.18 – VI MENN
"Hemmer kreft" – Karl-Henning Kalland

CCBIO 2018 - In the media

19.03.18 – LMI NYHETER
"Fem kjappe om kliniske studier" – Bjørn Tore Gjertsen

15.03.18 – LMI NYHETER
"Få kliniske studier gjør at norske pasienter ikke får rask nok tilgang til «state of the art»-behandling" – Bjørn Tore Gjertsen

06.02.18 – WORLD HEALTH NETWORK
"Drug For Tapeworm May Fight Prostate And Colon Cancer" – Karl-Henning Kalland

03.02.18 – DAGBLADET
"Gjennombrudd i kreftforskningen" – Lars A. Akslen

31.01.18 – HELSE BERGEN NEWS
"Kjempestas å få pris" – Katharina Bischof

26.01.18 – VOX PUBLICA
"Niels Chr. Geelmuyden: Pillebefinnende (podkast og video) – Hvilke interesser styrer utviklingen av kunnskap om legemidlene og deres virkninger?" – Roger Strand

26.01.18 – VI OVER 60
"Krefthemmende parasittmedisin" – Karl-Henning Kalland

22.01.18 – VI OVER 60
"Alderen du er mest utsatt for brystkreft" – Fanny Pélissier

06.01.18 – CORDOBA BUENAS NOTICIAS ARGENTINA
"Un fármaco utilizado contra los parásitos intestinales muestra eficacia contra el cáncer de próstata y colon" – Karl-Henning Kalland

Mini Biographies:

Mini Biographies:
PhD Candidates and Postdocs 2018

AHMED, ISRAA ABDULRHMAN
MS in dental surgery from the University of Khartoum, with clinical specialty in conservative dental medicine. Israa completed her PhD in 2018 at the University of Bergen in the Costea group, where she worked on identification of prognostic biomarkers for oral squamous cell carcinoma, studying human samples and experimental models.

ALAM, JAHEDUL
MS in biomedical sciences from Bonn, Germany, and is currently a PhD candidate in the Gullberg group. His research project aims to further characterize integrin α11 expression and function.

ANANDAN, SHAMUNDEESWARI
MSc in biotechnology and is currently a PhD (ESR) candidate in the INOvA group under Professors Bjørge and McCormack. Her research focus is using single cell mass cytometry by time of flight (CyTOF) to mine the ovarian tumor microenvironment with prospective exploitation of novel biomarkers and developing preclinical animal models towards precision medicine in ovarian cancer.

ASKELAND, CECILIE
MD from the University of Bergen, and works as a pathologist at the Department of Pathology, Haukeland University Hospital. She is currently a PhD candidate in the Akslen group, studying tissue-based biomarkers in aggressive subgroups of breast cancer with emphasis on tumor-stroma crosstalk.

AZEEM, WAQAS
MS in molecular biology from the University of Skövde, Sweden. He has been a PhD fellow in the Kalland group since 2014, and completed his PhD in June 2018 with the dissertation "Regulatory patterns in prostate cell differentiation – investigation of transcription factors AR, GATA2 and NKX3-1." Waqas is currently a postdoc in the Kalland group.

BENTSEN, PÅL TORE
MD from the University of Bergen and currently a PhD candidate in the Gjertsen group. His research is focused on acute graft-versus-host disease (aGVHD) after allogeneic hematopoietic stem cell transplantation, with a special emphasis on corticosteroid refractoriness. Using high-dimensional single cell analysis, the aim is to gain insights into basic disease biology and mechanisms of treatment responses.

BERG, HEGE FREDRIKSEN
MS in molecular medicine from the University of Essex. She is currently a PhD candidate in the Krakstad group and the main focus of her PhD project is to establish organoids as a preclinical model in endometrial cancer. Organoids will be used in drug testing studies both as an *in vitro* model and *in vivo* by generating organoid-derived PDX models.

BERGSJØ, LOUISE EMBLEM
MS in chemistry from the University of Bergen and has since August 2017 been a PhD student in the Haug group, with Emmet McCormack and Ole Heine Kvernenes as co-supervisors. Her PhD project focuses on making peptides for PET, with an aim to develop a new method for radiolabeling of bioactive molecules.

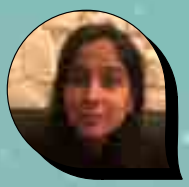
BIRKELAND, EVEN
MS in medical cell biology and a PhD on mutations and genetic alterations in endometrial cancer, both at the University of Bergen. He was until 2018 a postdoc in the Akslen group, doing research in the field of cancer proteomics, especially related to breast cancer subtypes and the tumor microenvironment.

BISCHOF, KATHARINA
MD and consultant in obstetrics and gynecology, working at the Women´s Clinic, Haukeland University Hospital. She is a PhD candidate in the McCormack and Bjørge groups and aims to complete her PhD in February 2019. Her PhD project focuses on gynecological high-grade serous carcinoma, the portrayal of the p53 isoform landscape and the development of a new preclinical tool for optical imaging in xenograft models.

BJÅNES, TORMOD KARLSEN
MD and senior consultant in clinical pharmacology at Haukeland University Hospital. Currently a PhD candidate in the Bergen Pharmacology and Pharmacy research group in collaboration with the SonoCure group (McCormack group). His main focus is on the nucleoside analogue gemcitabine in pancreatic cancer, with special emphasis on intracellular drug metabolite kinetics following sonoporation.

BØRRETZEN, ASTRID
MD from the University of Bergen. She is currently a PhD candidate in the Akslen group (main supervisor Professor Ole J. Halvorsen). Her research project is focused on epithelial-mesenchymal transition, angiogenesis and molecular markers in aggressive prostate cancer.

CHEN, YING
MD with specialty in pathology, currently head of department and chief consultant at the Department of Pathology, Oslo University Hospital. She has since 2015 been a PhD student in the Akslen group. Her PhD project focuses on the tumor microenvironment, aiming to identify the relationship between tumor-infiltrating lymphocytes, vascular invasion and stromal elastosis in breast cancer.



DAS, RIDHIMA
Certified dental surgeon from India with an MS in experimental oral pathology from Queen Mary University London, UK. She is currently a PhD candidate in the Costea group. Her research project is focused towards therapy and bone regeneration in cancer patients using targeted nanodiamonds.

Mini Biographies: PhD Candidates and Postdocs 2018

DAVIDSEN, KJERSTI TEFRE
MD from the University of Bergen and is currently doing her PhD in the Lorens and Straume groups. Her PhD project focuses on Axl mediated resistance to targeted therapy and immunotherapy, with an aim to increase understanding of the contexts where targeting Axl could enhance therapeutic benefit.

DE GARIBAY, GORKA RUIZ
PhD in biochemistry from the Complutense University of Madrid. Since 2017 he is a postdoctoral researcher in the McCormack group. His research is focused on the development of preclinical models of pancreatic ductal adenocarcinoma derived from patients.

DHAKAL, SUSHIL
BS from Anglia Ruskin University, UK, and an MS in biomedical sciences from the University of Bergen. He is currently a PhD student in the Lorens group, with a project that aims to understand the immune interplay between the type 1 interferons and the receptor tyrosine kinase Axl in tumor cell plasticity and immunotherapy resistance.

DHAKAL, SUSHMA PANDEY
BDS from BPKIHS, Dharan, Nepal and an MDS from MCODS, Manipal University, Karnataka, India. She is currently a PhD candidate at the University of Oslo, jointly with the Costea group at CCBIO. Her research project aims at identifying prognostic biomarkers in oral cancer and potentially malignant disorders, particularly focusing on the prognostic role of the S100 A14 protein on progression and differentiation of OSCC, and proliferation related biomarkers in recurrent leukoplakia.

DILLEKÅS, HANNA
MD from Linköping University, Sweden. She is currently a PhD candidate in the Straume group. Her research is focused on tumor dormancy and how tissue trauma and wound healing can stimulate escape from dormancy to produce overt metastatic disease in breast cancer.

DIMITRAKOPOULOU, KONSTANTINA
MS in biomedical engineering and a PhD, both from the University of Patras, Greece. Her doctoral thesis focused on complex disease analysis through systems biology approaches. She was until 2018 a postdoc in the Jonassen and Akslen groups with a focus on deconvolution studies of the breast cancer microenvironment.

DONGRE, HARSH
MTech in bio-nanotechnology from India, and has since 2017 been a PhD candidate in the Costea group. His research project focuses on the role of miRNAs in tumor-stroma interaction in squamous cell carcinomas with special emphasis on targeting altered miRNAs and proteins using functionalized nanodiamonds.

DOWLING, TARA HELEN
BS in biology and MS in biomedicine, both from the University of Bergen. She has since 2016 been a PhD candidate in the McCormack and Gjertsen groups. Her PhD project focuses on developing novel hBMSC derived scaffold mouse models and identifying potential treatable biomarkers, with an aim to aid the development of new therapeutic modalities for myeloid leukemias.

DYBVIK, JULIE
MD from the University of Bergen and has been working as a resident in radiology in the Department of Radiology, Haukeland University Hospital, since she completed her degree. She is currently a PhD candidate in the Krakstad group, working on functional imaging for individualized treatment of uterine cancer.

EDELMANN, REIDUNN
MD and PhD in 2014 on vascular phenotypes in inflammation, both from the University of Oslo. She is now a postdoc in a joint collaboration between the Östman and Akslen groups, where her research project aims at identifying new biomarkers in aggressive breast cancer through multiplexed profiling of the tumor vasculature.

ERTSÅS, HENRIETTE CHRISTIE
MS in virology from the University of Bergen. She completed her PhD in April 2018 in the Lorens group, working on the effects of aging on microenvironment-contextual epithelial cell signaling. Her research goal in the PhD was to understand how the microenvironment determines cell fate and tumor progression.

FASMER, KRISTINE ELDEVIK
MS in physics from the University of Oslo and works as a medical physicist at the Department of Radiology, Haukeland University Hospital. Since 2017 she has been a PhD candidate in the Krakstad group, working on functional imaging for individualized treatment of uterine cancer.

ENGEN, CAROLINE BENEDICTE NITTER
MD from the University of Bergen, and she currently works on her PhD project in the Gjertsen group. Caroline's research project aims to elucidate aspects of clonal heterogeneity and clonal evolution in acute myeloid leukemia, with specific focus on possible translational implications.

ENGERUD, HILDE
MD from the University of Bergen. She is currently a PhD candidate in the Krakstad group. Her research project aims to explore molecular biomarkers in endometrial cancer in order to better predict prognosis and guide therapy.

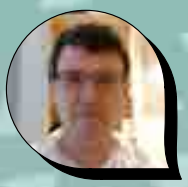
ESPEDAL, HEIDI
PhD from the University of Bergen from 2015, and has since been the manager of the preclinical PET/CT facilities at MIC. From November 2018, she combines the position at MIC with a 50 % postdoc in the Bergen Gynecologic Cancer Group. Her research focuses on imaging of preclinical gynecological models and image analyses, with an aim to identify new imaging biomarkers to facilitate targeted therapy in gynecological cancers.

FINNE, KENNETH
MS in molecular biology from the University of Bergen, and completed in 2018 a PhD on proteomic changes in hypertensive kidney disease. He is now a postdoc in the Akslen group. His research interests are in the field of cancer proteomics, especially related to breast cancer subtypes and the tumor microenvironment.

Mini Biographies: PhD Candidates and Postdocs 2018

FONNES, TINA
Has a veterinary degree from NVH, and was until November 2018 a PhD candidate in the Krakstad group and explored cell lines, clinical samples and mouse models of endometrial cancer with special attention to imaging protocols and therapeutic studies. Her PhD work focused on preclinical models and molecular biomarkers – tools to improve treatment in endometrial carcinoma.

FORSSE, DAVID
MD and a gynecologist, currently a PhD candidate in the Bergen Gynecologic Cancer Research Group studying tissue biomarkers in endometrial and cervical cancer.



GELEBART, PASCAL
PhD in the field of immuno-onco hematology from the Université Paris VII, Centre Hayem, Hôpital Saint Louis in France; in 2018 a postdoc in the McCormack laboratory with primary research focus on the development of preclinical models of leukemia and lymphoma. He has since obtained a researcher position in McCormack's group.

GUERREIRO, EDUARDA
MS in biomedical sciences from the University of Algarve. She is currently a PhD student in the Institute of Oral Biology, University of Oslo, connected to the Costea group at CCBIO. Her PhD project focuses on extracellular vesicles from oral cancer with an aim to understand their role in tumor progression.

GULLAKSEN, STEIN-ERIK
MS in nano-science and a BS in nano-technology, both from the University of Bergen. He has been a PhD student in the Gjertsen group, and completed his PhD on single cell signaling and immune profiles in chronic myeloid leukemia in 2018. Stein-Erik moved subsequently on to a researcher position in the McCormack group.

HA, TRUNG QUANG
MD from Vietnam, holds an MS in medical biology from the University of Bergen and is currently a PhD candidate in the Gjertsen group. His research focus is on developing p53-independent and p53-dependent novel therapies for the treatment of acute myeloid leukemia.

HAJJAR, EHSAN
MS in medical cell biology from the University of Bergen, and has since 2015 been a PhD candidate in the Gjertsen group. His project focuses on the modulation and function of p53 protein isoforms in acute myeloid leukemia using proteomic assays, examining the modulation of p53 protein isoforms in the leukemic cells treated by the Axl inhibitor agent BGB324 and Crm1 inhibitor drug KPT-330.

HALLE, MARI KYLLESØ
MS in molecular biology from NULS and a PhD from the University of Bergen. She is currently a postdoc in Camilla Krakstad's group working on gynecological cancer. Her main focus is to characterize targetable molecular alterations driving aggressive cervical carcinoma.

HAUGSE, RAGNHILD
MS in pharmacy from the University of Oslo. She is currently a PhD candidate in the McCormack group and her research focuses on increased drug delivery and therapeutic efficacy of cancer therapy by the use of ultrasound and microbubbles (sonoporation).

HELLESØY, MONICA
MS in human physiology and completed her PhD at the University of Bergen in 2013. She is currently a postdoc in the Gjertsen group. Her research focuses on characterizing the effects of novel targeted therapies for acute myeloid leukemia, mainly through single cell analyses of samples collected from patients in clinical trials.

HUA, YAPING
MS in medical chemistry from Shanghai Jiaotong University, China, and is currently a PhD candidate in the Kalland group. Her project focuses on the discovery of leading compounds and their molecular targets in prostate tumor-initiating cells as well as STAT3 inhibitors in autologous immature dendritic cells.

HUGDAHL, EMILIA
MD from the University of Bergen in 2006. Emilia was a PhD fellow in the Akslen group from 2014, and completed her PhD in April 2018. Her project focused on biomarkers for aggressive cutaneous melanoma, especially related to pro-liferation, BRAF mutations, and metastatic spread. Emilia continued in the Akslen group after completing her PhD, in a position as researcher.

JACOB, HAVJIN
MS in molecular medicine from NTNU and a PhD from the University of Bergen, and is currently a postdoc in the Gynecological Cancer Research Group. Her research is focused on molecular markers in endometrial cancer and their association with functional imaging parameters for individualized cancer treatment.

JEBSEN, NINA LOUISE
MD from the University of Trondheim, and is a specialist in oncology with a PhD gained in 2013 on adjuvant radiotherapy in soft tissue sarcoma investigating prognostic factors for local recurrence. Currently a postdoc in the Gjertsen group in a strategic project on personalized medicine focusing on biomarkers in clinical studies of advanced cancer. Of particular interest is liquid biopsy during the course of therapy with drugs targeting the tumor microenvironment, such as immune cells.

KANG, JING
MS in dermatology and venereology from Shandong University, and another MS in biomedicine from the University of Bergen. She holds an MD from the Taishan Medical University, and is since 2016 a PhD candidate in the Lorens group. Her PhD project focuses on the role of Axl signaling in tumor metastasis and anti-tumor immune evasion, with an aim to study how Axl signaling affects melanoma metastasis and how Axl receptor cell signaling leads to anti-tumor immune evasion.

KJØLLE, SILJE
MS in molecular biology from the University of Bergen, and currently a PhD candidate in the Akslen group. Her research project is focused on hypoxia in breast cancer. The project aims to explore the hypoxia response at the proteomic level and effects of hypoxia on the tumor microenvironment and processes involved in tumor progression.

KLEINMANNS, KATRIN
MS in biomedicine from Hannover Medical School, Germany, and started her PhD in the INovA group under supervision of Professors McCormack and Bjørge in 2016. Her project focuses on the development of immunocompetent patient-derived xenograft model of high-grade serous ovarian cancer, aiming to further improve therapeutic interventions by optimizing image guided surgery and testing immunotherapies.

KLINGEN, TOR AUDUN
MD from Århus University, Denmark. He was a PhD fellow in the Akslen group from 2014, and completed in February 2018 his PhD on vascular invasion by tumor cells, and other prognostic factors in a population-based breast cancer study. He is currently chief attending physician at Vestfold Hospital, and also a researcher in the Akslen group.

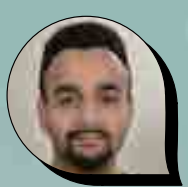
LEITCH, CALUM
Graduated from the University of Glasgow in 2012 with a Msci degree in molecular and cellular biology. Since 2012 he has been a PhD candidate in the Gjertsen group. His PhD focuses on the identification and repurposing of approved medicines for therapy development in acute myeloid leukemia. Particular emphasis is placed on mechanistic studies to determine likely responders in patient sub-groups.

LOTSBERG, MARIA LIE
MS in nanoscience from the University of Bergen and is currently a PhD candidate in the Lorens and Akslen groups. Her research project is focused on how the tumor microenvironment and cancer cell plasticity contributes to acquired therapy resistance in non-small cell lung cancer models with a special focus on the Axl receptor tyrosine kinase.

LUÍS, ANA BEATRIZ MATEUS D'AVÓ
MS in economics from the Nova School of Business and Economics, Portugal. She is currently a PhD candidate in the Health Economics Group, working on the cost-effectiveness of biomarkers in the Norwegian healthcare system and on the incentives of pharmaceutical firms to invest in R&D of drugs with biomarkers.

LURA, NJÅL
MD with background in internal medicine and radiology. He is now working on a PhD project in the Bergen Gynecologic Cancer Group, featuring precision imaging in patients with uterine cervical cancer. The project aims to explore potential imaging biomarkers that predict advanced tumor stages, metastases and reduced survival in uterine cervical cancers.

MADELEINE, NOELLY
MS in biochemistry and a PhD in bioinformatics, both from the University of la Réunion. She has since 2018 been a postdoc in the Lorens group. Her research focuses on generating and analyzing high-dimensional mass cytometry datasets to measure AXL-mediated tumor-immune interactions, with an aim to determine how AXL regulates tumor-immune crosstalk in the context of targeted therapy and immunotherapy.



MOHAMED, HASSAN ABDEL RAOUF-ALI
BDS from the University of Science and Techonology in Sudan, and an MPhil in oral sciences from the University of Bergen. He is currently a PhD candidate in the Mustafa and Costea groups. His MPhil focused on the expansion of mesenchymal stem cells under different expansion conditions, and his current PhD work is focused on analysis of induced pluripotent stem cells generated from fibroblasts from different sources.

MOHAMED, NAZAR
Dentist and dental microbiologist, holds an MS in molecular medicine from the University of Khartoum, Sudan. He has since 2015 been a PhD student in the Costea group. His PhD project focuses on characterization of the salivary mycobiome and the patterns of volatile organic compounds in the exhaled breath of patients with oral squamous cell carcinoma. He is also exploring the validity for clinical application of an electronic nose device, as a rapid and cost-effective screening tool for oral cancer (OSSC).

MOHAMED, NUHA
MS in periodontics from the University of Khartoum and has since 2016 been a PhD candidate in the Costea group. Her PhD project focuses on oral microbiome identification, with an aim to correlate it with the inflammatory host reaction and survival of oral squamous cell carcinoma patients from Sudan.

MOSES, MUSIIME
MS in biomedicine from the University of Bergen, and is currently a PhD candidate in the Gullberg group. His PhD project is focused on the role of integrin α11 in fibrosis and characterization of new tools for anti-fibrotic research.

PILSKOG, MARTIN
MD at the Department of Oncology, Haukeland University Hospital, and a PhD candidate in the Straume and Akslen groups. He investigates the roles of interleukin 6 and interleukin 6 receptor as biomarkers in relation to anti-angiogenesis treatment of metastatic renal cell carcinoma.

RAJTHALA, SAROJ
BDS in biochemistry and an MPhil in Medical Cell Biology from University of Bergen. He has since 2014 been a PhD candidate in the Costea group. His research focuses on identification of a miRNA signature in the tumor stroma that can be used as prognostic factor and for therapeutic intervention.

RAMNEFJELL, MARIA
MD from the University of Bergen, and completed her PhD in 2018 in the Akslen group. Her thesis focused on molecular and clinico-pathologic characteristics of non-small cell lung cancer, exploring novel biomarkers and potential treatment targets, with focus on the tumor microenvironment including activated angiogenesis. She currently works as a pathologist at the Department of Pathology, Haukeland University Hospital, and is also a researcher in the Akslen group.

RANE, LALIT SHIRISH
BS in veterinary medicine from Bombay Veterinary College, Mumbai, India, an MS in molecular biology from the University of Skövde, Sweden and a PhD from Karolinska Institutet, Sweden. He is currently a postdoc in the Gjertsen group focusing on investigating alternative splicing of P53 gene in human acute myeloid leukemia with aim to better understand AML disease progression and treatment stratification through P53 alternative splicing.

SCHUSTER, CORNELIA
MD and a Dr. Med, both from the Friedrich-Alexander University of Erlangen, Nurnberg, Germany. She gained a PhD on predictive markers in metastatic melanoma in 2016 from the University of Bergen and is now a postdoc in the Straume and Akslen groups. Her research focus is on biomarkers in melanoma treatment and she is a co-investigator in a clinical trial for patients with metastatic melanoma.

Mini Biographies: PhD Candidates and Postdocs 2018

SEMBAJWE, LAWRENCE FRED
Holds a veterinary degree and an MS in physiology from the Makerere University College of Health Sciences in Kampala, Uganda. Has since 2015 been a PhD fellow in the Gullberg group, where he completed his PhD in August 2018 on EXT proteins and their role in heparan sulfate assembly and tumor biology.

SEO, MIKYUNG KELLY
Economist with work experiences in international organizations and consultancies. She holds an MS in health policy, planning and financing from LSE and LSHTM, and is currently a PhD candidate in health economics focusing on economic evaluations of cancer biomarkers under the supervision of Professor John Cairns at LSHTM.

SHAFIEE, SAHBA
MS in biomedical cell biology from the University of Bergen, and is currently a PhD student in the Gjertsen and McCormack groups. Her PhD work is focusing on translational development of preclinical models and therapies in myelodysplastic syndromes (MDS).

SKAVLAND, JØRN
Holds a technical education in electronics and automation, an MS in immunology, and completed in 2013 a PhD at the University of Bergen on risk stratification and therapy response monitoring by phosphoprotein profiles in acute myeloid leukaemia. He was a postdoc in the Gjertsen group until 2018, where he monitored and evaluated signaling related patterns in leukemia.

SLETTA, KRISTINE YTTERSIAN
BS in biomedical science, University of the Sunshine Coast, Australia and an MS in biomedicine, University of Bergen. She is currently a PhD student in the Gjertsen group, working on tumor-stroma interactions and employing different *in vitro* and *in vivo* models for the preclinical development of small molecule kinase inhibitors towards CSF1R (colony stimulating factor 1 receptor) in acute myeloid leukemia.

SMELAND, HILDE YTRE-HAUGE
MD from the University of Bergen, currently a PhD candidate in the Akslen group. Her project is focused on the role of integrin α11β1 in breast cancer; both in experimental models and in human breast cancer.

STIGEN, ENDRE
MS in medical cell biology. He was a PhD candidate in the McCormack group focusing on nitroreductase (NTR) reporter gene expression and the development of preclinical Sonoporation-directed enzyme prodrug therapy (SDEPT) towards pancreatic cancer. He moved during 2018 on to the Lorens group as staff engineer.

SULIMAN, SALWA
BDS from the University of Khartoum, Sudan, a PhD from the University of Bergen, and has been a postdoc in the Costea group since February 2017. Her research focuses on stem cells and functionalized materials targeting therapy of oral cancer and bone regeneration.

TORKILDSEN, CECILIE FREDVIK
MD from the University of Bergen and a PhD candidate in the Precision Medicine in Ovarian Cancer Research Group. Her focus is surgical management of ovarian cancer with the aim to identify clinical and molecular predictors of successful surgery.

TRANVÅG, EIRIK JOAKIM
MD from the University of Bergen and is currently a PhD candidate in the Global Health Priorities Research Group and part of the ELSA team. He investigates how cancer biomarkers can inform better and fairer priority setting in health care, and in particular how the personalization of cancer medicine can alter priority setting practice. His broader research interest are medical ethics and health care justice, drug pricing and reimbursement, and clinical decision making.

THOMSEN, LIV CECILIE VESTRHEIM
MD, specialist in obstetrics and gynecology, and holds a PhD from the University of Bergen on the genetic background of complex diseases. Since 2017 she has been a postdoc in the Gjertsen group, with focus mainly on mass cytometry (CyTOF) analyses; to develop antibody panels and thereby detect immune effects and checkpoint inhibitor responses as well as rare circulating tumor-associated cells in patient-derived materials. Her job also encompasses analyses of data from early phase clinical trials on prostate and ovarian cancer.

VIÑEGRA, ELVIRA GARCÍA DE JALÓN
BS in chemistry and a Master in organic synthesis and medicinal chemistry from the University of Bergen. She is now pursuing her PhD in the McCormack group and her research focuses on the development and pre-clinical evaluation of site-specific dyes allowing for accurate tumor development evaluation using optical and PET/CT imaging.

XENAKI, VICTORIA
DDS from the I.M. Sechenov First Moscow State Medical University and has since 2016 been a PhD student in the Costea group. Her PhD project focuses on nanotechnology in dentistry, with an aim to evaluate attitude of dental health care workers with regard to the use of nanotechnology and assess toxicity of nanoparticles used in dentistry in the context of nanosafety.

YTRE-HAUGE, SIGMUND
MD from the University of Bergen, and currently a PhD student in the Bergen Gynecologic Cancer Group. His PhD project focuses on preoperative tumor texture analysis from MRI, with an aim to identify new imaging parameters for better preoperative risk-classification of endometrial carcinomas.

ÅSE, HILDEGUNN SIV
MD and radiologist who holds an MS in health economics from the University of Bergen. Currently a PhD student in the Bergen Gynecologic Cancer Group. Her PhD project focuses on digital breast tomosynthesis (3D-mammography) in screening, with data from the Tomosynthesis Trial i Bergen (the To-Be-trial), focusing on detection rates, reading times, doses and other relevant issues, comparing results after screening with digital mammography (2D) versus digital breast tomosynthesis.

FACTS AND FIGURES 2018

PERFORMANCE INDICATORS

	2013	2014	2015	2016	2017	2018	TOTAL
PUBLICATIONS	76	71	77	85	94	81	484
COMPLETED PHDS	5	6	3	10	12	9	45
EXTERNAL FUNDING MNOK	7.2	21.9	22.5	36.0	34.0	32.1	154
MEDIA APPEARENCES	39	11	32	31	54	40	207

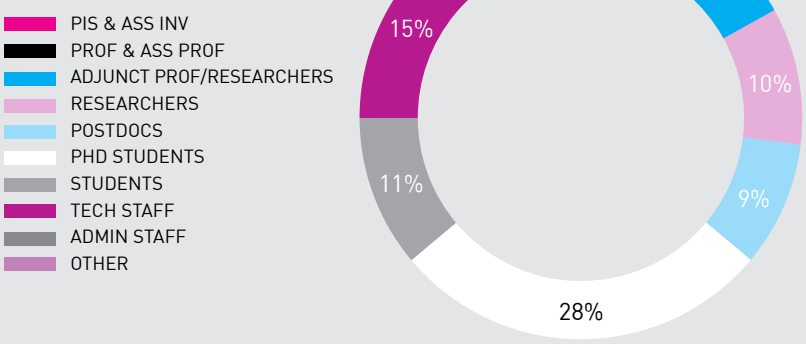
The table illustrates CCBIO's performance for 2013-2018. The scientific production is high. The reduction from 2017 is due to the first round of CoE financed PhDs and postdocs now having concluded their projects, publishing predominantly in 2016-2017. The influx of external funding is very good and numbers illustrate external funds consumed for the respective year.

GENDER DISTRIBUTION
(HEADCOUNT)

TOTAL: 209 PERSONS

In general, of the 209 persons involved in CCBIO, the gender distribution is female dominating with 67%. Among PhD students and postdocs 65% and 64% are females respectively. This tendency shifts among professors and associate professors, where 39% are female. However, recruitment of excellent female staff to enlarge the CCBIO group of investigators has considerably lowered the male proportion in this group with 29% now being female. By attaining a more balanced gender distribution in its top tire, CCBIO aims to put all available talent to its best use. Hence, CCBIO improves its gender balance without affirmative action or compromising on excellence.

CCBIO STAFF OVERVIEW
(HEADCOUNT)

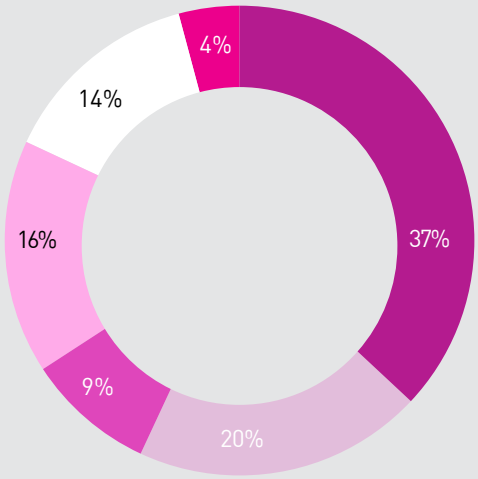


TOTAL: 211 PERSONS

CCBIO has a quite balanced composition of junior and senior researchers. In the coming years, CCBIO will increase the amount of postdoctoral positions, in order to increase the chances for major breakthroughs, which depends more upon postdocs than PhDs. CCBIO has upgraded younger investigators to full PI and associate PI status. These investigators, predominantly female, and further newly recruited investigators in the years to come, will ensure a continuation of high impact CCBIO projects after 2023. CCBIO's international network of 13 adjunct professor and researchers ensures excellent access to high-level collaboration, advice and tuition for CCBIO's researchers, younger researchers and PhDs respectively. One new member was recruited in 2018, Professor Ian Mills from the University of Oxford. The majority of CCBIO's staff is of Norwegian origin (61%) and an equal amount originates from African and Asian countries (20%) and other Western countries (19%).

FUNDING
(FUNDS USED IN 2018)

- UIB
- RCN CoE
- RCN PROJECTS
- OTHER PUBLIC FUNDING
- PRIVATE FUNDING
- INTERNATIONAL FUNDING

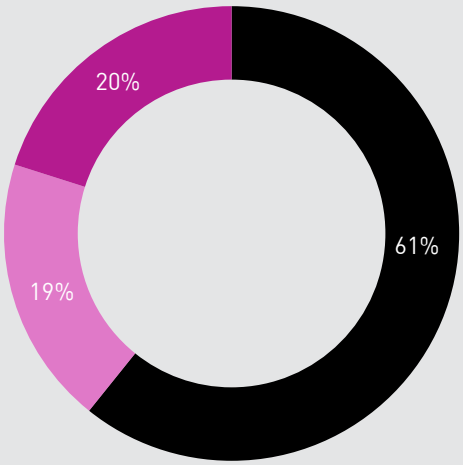


TOTAL = 74 MILL NOK

Total funds used in 2018 were 74 MNOK, of which 57% is the RCN CoE funding and own funding from UiB. The external funding consumed was 32.1 MNOK. This is 2.6 times the budgeted amount and illustrates a high success rate with public and private funding agencies. We expect to see an increase in external funds used, as CCBIO starts using its new technology for deep tissue profiling. This technology is expensive in use, but we expect it to yield high output scientifically.

INTERNATIONALIZATION
(STAFF COUNTRY OF ORIGIN)

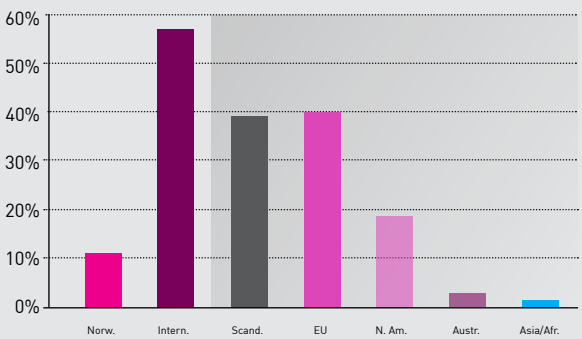
- NORWAY
- EUROPEAN & WESTERN COUNTRIES
- AFRICA & ASIA



CCBIO is an international CoE with 39% of its staff being of foreign nationalities. Among PhDs and postdocs, 47% and 42% originate from outside of Norway. Among CCBIO's senior researchers, 40% are foreign nationals 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 substantial amount of scientific publications with international contributors, with 59% of CCBIO's publications having at least one co-author from institutions abroad. International co-authorship has much stronger prevalence than co-authorship by researchers from other Norwegian universities (12% of publications). Subdividing the international co-authorships into regions (grayed out background color) demonstrates that CCBIO collaborates with institutions from most major world regions. By comparing the "International, over all"-column with the aggregate values of the five columns to the right, one can easily discern that many of CCBIO's international publications have co-authors from more than one region, being truly multilateral collaborations across world regions.

INTERNATIONALIZATION
(STAFF CO-AUTHORSHIP)

- NORWAY, NON-BERGEN
- INTERNATIONAL, OVER ALL
- SCANDINAVIA
- EUROPEAN UNION
- NORTH AMERICA
- AUSTRALIA
- ASIA & AFRICA



Complete List of Personnel at CCBIO 2018

Name	Position	Academic title	Group
Aae, Liv Rebecca Arnedatter	Senior Executive Officer	MA	Administration
Ahmed, Israa	PhD student	DDS	Costea
Akslen, Lars A.	Professor, Director, Principal Investigator	MD, PhD	Akslen
Amant, Frédéric	Adjunct Professor	MD, PhD	CCBIO
Andresen, Vibeke	Senior Researcher	MS, PhD	Gjertsen
Anandan, Shamundeeswari	PhD student	MSc	McCormack/Bjørge
Andreassen, Kim	Advisor		Administration
Andresen, Vibeke	Senior Researcher	MSc, PhD	Gjertsen
Ardawatia, Vandana	Senior engineer	PhD	Akslen
Arnes, Jarle	Senior Consultant	MD, PhD	Akslen
Askeland, Cecilie	PhD student	MD	Akslen
Askildsen, Jan Erik	Professor, Associate Investigator	MA, PhD	Askildsen
Augestad, Grete	Study nurse		Bjørge
Azeem, Waqas	Postdoc	MS, PhD	Kalland
Aziz, Sura Mohammed	Senior Researcher	MD, PhD	Akslen
Bachmann, Ingeborg	Professor	MD, PhD	Akslen
Bakke, Ragnhild Maukon	Medical student		Kalland
Bedringaas, Siv Lise	Chief Engineer	MSc	Gjertsen
Bentsen, Pål Tore	PhD student	MD	Gjertsen
Berg, Hege Fredriksen	PhD student	MSc	Krakstad
Berge, Sissel Vik	Chief Engineer		Lorens
Bergsjø, Louise Emblem	PhD student	MSc	McCormack
Beroukhim, Rameen	Adjunct Researcher	MD, PhD	CCBIO
Birkeland, Even	Postdoc	PhD	Akslen
Bischof, Katharina	PhD student	MD	Bjørge
Bjørge, Line	Professor, Associate Investigator	MD, PhD, MBA	Bjørge
Bjånes, Tormod Karlsen	PhD student	MD	McCormack
Bougnaud, Sébastien	Researcher	PhD	Lorens
Bourdon, Jean-Christophe	Adjunct Researcher	MS, PhD	CCBIO
Bredholt, Geir	Researcher	PhD	McCormack

Name	Position	Academic title	Group
Breines, Ragna	Administrative Leader	Siv.ing, PhD	Administration
Brekken, Rolf	Adjunct Professor	MD, PhD	CCBIO
Bremer, Anne Blanchard	Researcher	MA, PhD	Strand
Brodal, Hans Petter	Staff Engineer	MSc	Gjertsen
Børretzen, Astrid	PhD student	MD	Akslen
Cairns, John	Adjunct Professor, Associate Investigator	MA, PhD	Cairns
Chen, Ying	PhD student	MD	Akslen
Chen, Ying Yi	Researcher		Lorens
Costea, Daniela Elena	Professor, Associate Investigator	DDS, PhD	Costea
Das, Ridhima	PhD student	DDS	Costea
Davidsen, Kjersti	PhD student	MD	Lorens/Straume
de Garibay, Gorka Ruiz	Postdoc	PhD	McCormack
de Montlaur, Constance de Villardi	Staff engineer	PhD	McCormack
Dhakal, Sushil	PhD student	MS	Lorens
Dhakal, Sushma Pandey	PhD student	DDS	Costea
Dillekås, Hanna	PhD student	MD	Straume
Dimitrakopoulou, Konstantina	Postdoc	MS, PhD	Jonassen/Akslen
D'Mello, Stacey Ann	Researcher	PhD	Lorens
Dongre, Harsh	PhD student	MSc	Costea/Bjørge
Dowling, Tara Helen	PhD student	MSc	Gjertsen/McCormack
Dybvik, Julie	PhD student	MD	Krakstad
Dyrkolbotn, Kjetil	Higher Executive Officer	MA	Administration
Edelmann, Reidun Jetne	Postdoc	MD, PhD	Akslen
Edvardsen, Britt	Chief Engineer		Krakstad
Eldevik, Kristine Fasmer	PhD student	MSc	Krakstad
Enge, Elisabeth	Study Nurse		Krakstad/Bjørge
Engelsen, Agnete	Researcher	MS, PhD	Lorens
Engen, Caroline Benedicte Nitter	PhD student	MSc, MD	Gjertsen/McCormack
Engerud, Hilde	PhD student	MD	Krakstad
Eriksen, May Gjerstad	Staff engineer	MSc	McCormack
Ertsås, Henriette	PhD student	MS	Lorens
Espedal, Heidi	Postdoc	MSc, PhD	Krakstad
Fagerholt, Oda Helen Eck	Student, pre-phd		Gjertsen
Fandalyuk, Zinayida	Staff engineer	MSc	McCormack
Finne, Kenneth	Postdoc	PhD	Akslen
Fonnes, Tina	PhD student	MedVET	Krakstad/McCormack
Forsse, David	PhD student	MD	Krakstad
Forthun, Rakel Brendsdal	Researcher	MSc, PhD	Gjertsen
Fosse, Vibeke	Veterinarian	DMV	McCormack
Fromreide, Siren	Chief engineer		Costea
Gabra, Hani	Adjunct Professor	MD, PhD	CCBIO
Gabrielsen, Tommy Staahl	Professor	MA, PhD	Askildsen
Garujel, Rashmi Chetri	Master student, pre-PhD	DDS	Costea
Gavasso, Sonia	Researcher	MSc, PhD	Gjertsen
Gelebart, Pascal	Postdoc	PhD	McCormack
Gjertsen, Bjørn Tore	Professor, Co-Director, Principal Investigator	MD, PhD	Gjertsen
Golburean, Olga	Master student, pre-PhD		Costea
Grønning, Mona	Chief Engineer		Gullberg
Guerreiro, Eduarda	PhD student	MS	Costea
Guldberg, Erik Andreas	Master student	BSc	McCormack
Gullaksen, Stein Erik	PhD student, then researcher	MSc, PhD	Gjertsen/McCormack
Gullberg, Donald	Professor, Principal Investigator	PhD	Gullberg
Ha, Trung Quang	PhD student	MD, MSc	Gjertsen
Haaland, Gry Sandvik	Researcher	MD, PhD	Straume
Hagen, Maria Helene	Dental student, pre-PhD		Costea
Hajjar, Ehsan	PhD student	MSc	Gjertsen
Haldorsen, Ingfrid Salvesen	Adjunct Professor	MD, PhD	Krakstad
Halle, Mari Kyllesø	Postdoc	MS, PhD	Krakstad
Hallseth, Gerd Lillian	Senior Engineer		Akslen
Halvorsen, Ole Johan	Professor	MD, PhD	Akslen
Haugse, Ragnhild	PhD student	MSc	McCormack
Heljasvaara, Ritva	Adjunct Researcher	MS, PhD	CCBIO
Hellesøy, Monica	Postdoc	MSc, PhD	Gjertsen

Name	Position	Academic title	Group
Hjelle, Sigrun Margrethe	Administrative support	MS, PhD	Gjertsen
Hoang, Hua My	Staff Engineer		Kalland
Hove, Elisabeth	Senior Executive Officer		Administration
Hovland, Randi	Senior researcher	MSc, PhD	Gjertsen
Hua, Yaping	PhD student	MS	Kalland
Hugdahl, Emilia	Researcher	MD, PhD	Akslen
Høgås, Mildrid Bønes	Senior Executive Officer		Administration
Høivik, Erling	Researcher	MS, PhD	Krakstad
Høysæter, Trude	Staff engineer		Gjertsen
Jacob, Havjin	Postdoc	MSc, PhD	Krakstad
Jacobsen, Martha Rolland	Dental student, pre-PhD		Costea
Jahedul, Alam	PhD student	MSc	Gullberg
Jebsen, Nina Louise	Postdoc	MD, PhD	Gjertsen
Johannessen, Anne Christine	Professor	MD, DDS, PhD	Costea
Jonassen, Inge	Professor, Associate Investigator	MS, PhD	Jonassen
Kalland, Karl-Henning	Professor, Principal Investigator	MD, PhD	Kalland
Kalvenes, May Britt	Senior Engineer	PhD	Akslen/Costea
Kang, Jing	PhD student	MD	Lorens
Karlsen, Ida	Staff engineer	MSc	McCormack
Kjølle, Silje	PhD student	MSc	Akslen
Kjørsvik, Øystein	Master student		Jonassen
Kleinmanns, Katrin	PhD student	MSc	McCormack/Bjørge
Klingen, Tor Audun	Researcher	MD, PhD	Akslen
Knutsvik, Gøril	Researcher	MD, PhD	Akslen
Kopperud, Reidun	Senior Engineer	MS, PhD	Gjertsen
Kotopoulis, Spiros	Senior researcher	PhD	McCormack
Krakstad, Camilla	Professor, Associate Investigator	MS, PhD	Krakstad
Kusche-Gullberg, Marion	Professor	PhD	Gullberg
LaBarge, Mark	Adjunct Professor	MS, PhD	CCBIO
Ladstein, Rita Grude	Associate Professor	MD, PhD	Akslen
Lam, Christina	Master student	BSc	McCormack
Langer, Anika	Researcher	PhD	McCormack
Leitch, Calum	PhD student	MSc	Gjertsen/McCormack
Liang, Xiao	Researcher	DDS, PhD	Costea
Litlabø, Hanne Bjelland	Student, pre-phd		Akslen
Litlekalsøy, Jorunn	Chief Engineer	MS, PhD	Costea
Lorens, Jim	Professor, Principal Investigator	MS, PhD	Lorens
Lotsberg, Maria Lie	PhD student	MS	Lorens
Lu, Ning	Senior Engineer	PhD	Gullberg
Luís, Ana Beatriz Mateus D'Avó	PhD student	MA	Askildsen
Lura, Njål	PhD student	MD	Krakstad
Løken, Geir Olav	Administrative Leader	Cand. Polit.	Administration
Madeleine, Noëlly	Postdoc		Lorens
Madissoo, Kadri	Senior Engineer		Krakstad
Manrikyan, Gayane	Guest researcher	DDS	Costea
McCormack, Emmet	Professor, Principal Investigator	PhD	McCormack
Mills, Ian	Adjunct Professor	MS, PhD	CCBIO
Mohamed, Fatima Ben	Master Student		Gullberg
Mohamed, Hassan Abdel Raof-Ali	PhD student	DDS	Costea
Mohamed, Nazar	PhD student	DDS	Costea
Mohamed, Nuha Gafaar	PhD student	DDS	Costea
Motzfeldt, Inga Kristine Flaaten	Master student	BSc	Gjertsen
Musana, Mary Gertrude	Master student		Jonassen
Musiime, Moses	PhD student	MSc, PhD	Gullberg
Myrvold, Madeleine	Medical student		Krakstad
Neppelberg, Evelyn	Adjunct Associate Professor	DDS, PhD	Costea
Nginamau, Elisabeth Sivy	Researcher	MD, PhD	Costea
Nguyen, Rebecca	Apprentice, lab technician		Gjertsen
Nilsen, Irmelin W.	Master student		Strand
Norheim, Ole Frithjof	Professor, Associate Investigator	MD, PhD	Norheim
Pantel, Klaus	Adjunct Professor	MD, PhD	CCBIO
Papian, Andrew	Guest researcher	MD	Costea
Pilskog, Martin	PhD student	MD	Straume/Akslen

Name	Position	Academic title	Group
Popa, Mihaela Lucia	Staff engineer	DVM	McCormack
Pridesis, Ann-Helen	Study nurse		Krakstad
Rajthala, Saroj	PhD student	MS	Costea
Ramnefjell, Maria	Researcher	MD, PhD	Akslen
Rane, Lalit Shirish	Postdoc	MSc, PhD	Gjertsen
Reed, Rolf	Professor	MD, PhD	CCBIO
Riise, Julie	Adjunct Associate Professor	MA, PhD	Askildsen
Rozmus, Ezekiel Richard	Master student	BSc	McCormack
Sabir, Misbah	Staff Engineer	MSc	Gjertsen
Safont, Mireia Mayoral	Staff engineer	BSc	McCormack
Schuster, Cornelia	Postdoc	MD, PhD	Akslen/Straume
Sembajwe, Lawrence Fred	PhD student	MS	Gullberg
Seo, Mikyung Kelly	PhD student	MA	Cairns
Shafiee, Sahba	PhD student	MSc	Gjertsen/McCormack
Skavland, Jørn	Postdoc	MSc, PhD	Gjertsen
Sletta, Kristine	PhD student	MSc	Gjertsen
Smeland, Hilde Ytre-Hauge	PhD student	MD	Akslen
Solheim, Marion	Advisor		Administration
Stefansson, Ingunn	Professor	MD, PhD	Akslen
Stenmarck, Mille Sofie	Medical student		Strand
Stigen, Endre	PhD student	MSc	McCormack/Lorens
Strand, Elin	Researcher	MSc, PhD	Krakstad
Strand, Roger	Professor, Principal Investigator	MS, PhD	Strand
Straume, Oddbjørn	Professor, Principal Investigator	MD, PhD	Straume
Suliman, Salwa	Postdoc	DDS, PhD	Costea
Sundøy, Silje Maria	Master student	BSc	McCormack
Svanøe, Amalie	Medical student, pre-PhD		Akslen/Wik
Sæle, Anna	Pre-PhD	MD	Akslen/Wik
Sødal, Marte	Master student		Krakstad
Sørlie, Therese	Adjunct Professor	MD, PhD	CCBIO
Tangen, Ingvild Løberg	Researcher	MPharm, PhD	Krakstad
Thiery, Jean Paul	Adjunct Professor	MD, PhD	CCBIO
Thodesen, Elisa Ulvøen	Staff engineer	MSc	McCormack
Thomsen, Liv Cecilie Vestrheim	Postdoc	MD, PhD	Gjertsen/Bjørge
Tislevoll, Benedicte Sjo	Student, pre-phd		Gjertsen
Torkildsen, Cecilie Fredvik	PhD student	MD	Bjørge
Tranvåg, Eirik Joakim	PhD student	MD	Norheim
Trovik, Jone	Professor	MD, PhD	Krakstad
Valen, Ellen	Study Nurse		Krakstad
Vidhammer, Eli Synnøve	Senior Executive Officer	BS	Administration
Viñegra, Elvira García de Jalón	PhD student	MSc	McCormack
Wangen, Rebecca	Staff Engineer	MSc	Gjertsen
Watnick, Randolph	Adjunct Researcher	MD, PhD	CCBIO
Werner, Henrica M. J.	Associate Professor	MD, PhD	Krakstad
Wik, Elisabeth	Associate Professor, Associate Investigator	MD, PhD	Akslen/Wik
Winge, Ingeborg	Senior Engineer	PhD	Akslen
Witsø, Solveig Lund	Senior Executive Officer	PhD	Administration
Xenaki, Victoria	PhD student	DDS	Costea
Xing, Zhe	Staff engineer	PhD, DDS, Mmed	McCormack
Ytre-Hauge, Sigmund	PhD student	MD	Krakstad
Zhuoyan, Zhang	Guest researcher	DDS	Costea
Östman, Arne	Adjunct Professor	MD, PhD	CCBIO
Øyan, Anne Margrethe	Senior scientist	MS, PhD	Kalland
Åse, Hildegunn	PhD student	MD	Krakstad

NEW STAFF MEMBERS IN THE CCBIO ADMINISTRATION

// GEIR OLAV LØKEN

Geir Olav Løken is back from a one year leave during which he was occupied full time hunting in Norway and subsequently sailing and kitesurfing in the Caribbean. He has taken up the reins as CCBIO's administrative leader after Ragna Breines who covered for him while he was away. As part of CCBIO's leader team, Geir Olav coordinates the administrative aspects of CCBIO's activities across its seven UiB departments and the center's interaction with collaborators nationally and abroad. Geir Olav has long experience in establishing and developing core facilities at the UiB and NTNU. He holds a Cand. Polit. degree from the UiB, published as a book in Germany, and he has added subjects from the Norwegian School of Economics (NHH) to his education.

// YVES AUBERT

Yves Aubert joined CCBIO in 2018 as a senior advisor for research and innovation (50 % position). Yves is a Swiss neuroscientist with 14 years of research and project management experience in academia and in the pharmaceutical and medical device industries. He obtained his MSc from the ETH Zürich, Switzerland, and his PhD from the Leiden University, The Netherlands. In between, he worked for 3 years at the University of Wisconsin-Madison, USA. He moved to Bergen in 2012, where he worked as post-doctoral researcher in the Bergen fMRI Group, and as principal scientist at a medical device start-up company. Yves has a successful track-record of securing industrial innovation grants, and he is now supporting CCBIO members in their grant application needs and innovation efforts.

// LIV REBECCA ARNEDATTER AAE

Liv Rebecca is originally Swedish, and has been resident in Norway since 1998. She holds a Bachelor in Economics and Administration and a Master of Management, both from the Norwegian Business School BI in Bergen. She is currently economy coordinator at the Department of Clinical Medicine (K1) and as part of CCBIO's financial team, she handles CCBIO's project portfolio at K1 together with CCBIO's economy coordinator, Mildrid Bønes Høgås. Liv Rebecca has since 2009 long experience in finance and management at departments of the University of Bergen, and has previous been working as accountant in private sector businesses. Liv Rebecca is a certified ski instructor, doing voluntary work teaching kids to ski in her spare time.

List of Publications

CCBIO - List of Publications 2018

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

Opsahl EM, Akslen LA, Schlichting E, Aas T, Brauckhoff K, Hagen AI, Rosenlund AF, Sigstad E, Grøholt KK, Mæhle L, Engebretsen LF, Jørgensen LH, Varhaug JE, Bjøro T. Trends in Diagnostics, Surgical Treatment, and Prognostic Factors for Outcomes in Medullary Thyroid Carcinoma in Norway: A Nationwide Population-Based Study. *Eur Thyroid J*. 2019 Jan;8(1):31-40. Epub 2018 Nov 8.

Yang Y, Wu L, Shu X … Long J (incl. Bjørge L). Genetic Data from Nearly 63,000 Women of European Descent Predicts DNA Methylation Biomarkers and Epithelial Ovarian Cancer Risk. *Cancer Res*. 2019 Feb 1;79(3):505-517. Epub 2018 Dec 17.

Tangen IL, Fasmer KE, Konings GF, Jochems A, Delvoux B, Xanthoulea S, Stokowy T, Strand E, Berg HF, Auriola S, Trovik J, Häkkinen MR, Haldorsen IS, ENITEC, Krakstad C, Romano A. Blood steroids are associated with prognosis and fat distribution in endometrial cancer. *Gynecol Oncol*. 2019 Jan;152(1):46-52. Epub 2018 Oct 26.

Mazloumi Gavgani F, Smith Arnesen V, Jacobsen RG, Krakstad C, Hoivik EA, Lewis AE. Class I Phosphoinositide 3-Kinase *PIK3CA*/p110α and *PIK3CB*/p110β Isoforms in Endometrial Cancer. *Int J Mol Sci*. 2018 Dec 7;19(12). pii: E3931. Review.

Tranvåg EJ, Norheim OF, Ottersen T. Clinical decision making in cancer care: a review of current and future roles of patient age. *BMC Cancer*. 2018 Dec 1;18(1):546.

Poirier M, Awale M, Roelli MA, Giuffredi GT, Ruddigkeit L, Evensen L, Stooss A, Calarco S, Lorens JB, Charles RP, Reymond JL. Identifying Lysophosphatidic Acid Acyltransferase β (LPAAT-β) as the Target of a Nanomolar Angiogenesis Inhibitor from a Phenotypic Screen Using the Polypharmacology Browser PPB2. *ChemMedChem*. 2019 Jan 22;14(2):224-236. Epub 2018 Dec 6.

Tangerås LH, Silva GB, Stødle GS, Gierman LM, Skei B, Collett K, Beversmark AL, Skråstad RB, Thomsen LCV, Bjørge L, Iversen AC. Placental inflammation by HMGB1 activation of TLR4 at the syncytium. *Placenta*. 2018 Dec;72-73:53-61. Epub 2018 Nov 2.

Brattås MK, Lilleeng K, Hovland R, Lægreid IJ, Vorland M, Leh F, Bruserud Ø, Gjertsen BT, Reikvam H. Philadelphia chromosome positive AML arising from JAK2-positive myelofibrosis. *Biomark Res*. 2018 Nov 21;6:33. eCollection 2018.

Kitajima K, Das R, Liang X, Neppelberg E, Johannessen AC, Costea DE, Igarashi M. Isolation and characterization of cells derived from human epithelial rests of Malassez. *Odontology*. 2018 Nov 26. [Epub ahead of print]

Kvalheim SF, Xenaki V, Kvalheim A, Lie SA, Marthinussen MC, Strand GV, Costea DE. Effect of glycerol on reconstructed human oral mucosa. *Eur J Oral Sci*. 2019 Feb;127(1):19-26. Epub 2018 Nov 19.

Holst F, Werner HMJ, Mjøs S, Hoivik EA, Kusonmano K, Wik E, Berg A, Birkeland E, Gibson WJ, Halle MK, Trovik J, Cherniack AD, Kalland KH, Mills GB, Singer CF, Krakstad C, Beroukhim R, Salvesen HB. *PIK3CA* Amplification Associates with Aggressive Phenotype but Not Markers of AKT-MTOR Signaling in Endometrial Carcinoma. *Clin Cancer Res*. 2019 Jan 1;25(1):334-345. Epub 2018 Nov 15.

Hua Y, Azeem W, Shen Y, Zhang S, Olsen JR, Øyan AM, Ke X, Zhang W, Kalland KH. Dual androgen receptor (AR) and STAT3 inhibition by a compound targeting the AR amino-terminal domain. *Pharmacol Res Perspect*. 2018 Nov 5;6(6):e00437. eCollection 2018 Dec.

Maynou L, Cairns J. What is driving HTA decision-making? Evidence from cancer drug reimbursement decisions from six European countries. *Health Policy*. Published online 20 November 2018.

Dimitrakopoulou K, Wik E, Akslen LA, Jonassen I. Deblender: a semi-/unsupervised multi-operational computational method for complete deconvolution of expression data from heterogeneous samples. *BMC Bioinformatics*. 2018 Nov 7;19(1):408.

Kusonmano K, Halle MK, Wik E, Hoivik EA, Krakstad C, Mauland KK, Tangen IL, Berg A, Werner HMJ, Trovik J, Øyan AM, Kalland KH, Jonassen I, Salvesen HB, Petersen K. Identification of highly connected and differentially expressed gene subnetworks in metastasizing endometrial cancer. *PLoS One*. 2018 Nov 1;13(11):e0206665. eCollection 2018.

Jørgensen KM, Færgestad Mosleth E, Hovde Liland K, Hopf NB, Holdhus R, Stavrum AK, Gjertsen BT, Kirkeleit J. Global Gene Expression Response in Peripheral Blood Cells of Petroleum Workers Exposed to Sub-Ppm Benzene Levels. *Int J Environ Res Public Health*. 2018 Oct 27;15(11). pii: E2385.

Reikvam H, Skavland J, Gullaksen SE, Hovland R, Gedde-Dahl T, Bruserud Ø, Gjertsen BT. Chronic Myeloid Leukemia Relapsing 25 Years after Allogenic Stem Cell Transplantation. *Case Rep Hematol*. 2018 Sep 23;2018:2045985. eCollection 2018.

Kirkeleit J, Riise T, Bjørge T, Christiani DC, Bråtveit M, Baccarelli A, Mattioli S, Hollund BE, Gjertsen BT. Maternal exposure to gasoline and exhaust increases the risk of childhood leukaemia in offspring - a prospective study in the Norwegian Mother and Child Cohort Study. *Br J Cancer*. 2018 Oct;119(8):1028-1035. Epub 2018 Oct 15.

Curry FE, Taxt T, Rygh CB, Pavlin T, Bjørnstad R, Døskeland SO, Reed RK. Epac1-/- mice have elevated baseline permeability and do not respond to histamine as measured with dynamic contrast-enhanced magnetic resonance imaging with contrast agents of different molecular weights. *Acta Physiol (Oxf)*. 2019 Mar;225(3):e13199. Epub 2018 Nov 2.

Strand R, Saltelli A, Giampietro M, Rommetveit K, Funtowicz S. New narratives for innovation. *Journal of Cleaner Production*, 197, 1849-1853, 1 October 2018.

Guerreiro EM, Vestad B, Steffensen LA, Aass HCD, Saeed M, Øvstebø R, Costea DE, Galtung HK, Søland TM. Efficient extracellular vesicle isolation by combining cell media modifications, ultrafiltration, and size-exclusion chromatography. *PLoS One*. 2018 Sep 27;13(9):e0204276. eCollection 2018.

Arteaga-Marrero N, Mainou-Gomez JF, Brekke Rygh C, Lutay N, Roehrich D, Reed RK, Olsen DR. Radiation treatment monitoring with DCE-US in CWR22 prostate tumor xenografts. *Acta Radiol*. 2018 Sep 19:284185118798167. [Epub ahead of print]

Schuster C, Akslen LA, Stokowy T, Straume O. Predictive value of angiogenic proteins in patients with metastatic melanoma treated with bevacizumab monotherapy. *J Pathol Clin Res*. 2019 Jan;5(1):53-62. Epub 2018 Nov 9.

Dmello C, Sawant S, Chaudhari PR, Dongre H, Ahire C, D'Souza ZC, Charles SE, Rane P, Costea DE, Chaukar D, Kane S, Vaidya M. Aberrant expression of vimentin predisposes oral premalignant lesion derived cells towards transformation. *Exp Mol Pathol*. 2018 Dec;105(3):243-251. Epub 2018 Sep 4.

Bruserud Ø, Costea DE, Laakso S, Garty BZ, Mathisen E, Mäkitie A, Mäkitie O, Husebye ES. Oral Tongue Malignancies in Autoimmune Polyendocrine Syndrome Type 1. *Front Endocrinol (Lausanne)*. 2018 Aug 17;9:463. eCollection 2018.

CCBIO 2018 - List of Publications

Håvik AL, Bruland O, Aarhus M, Kalland KH, Stokowy T, Lund-Johansen M, Knappskog PM. Screening for viral nucleic acids in vestibular schwannoma. *J Neurovirol*. 2018 Dec;24(6):730-737. Epub 2018 Aug 30.

Konings GF, Saarinen N, Delvoux B, Kooreman L, Koskimies P, Krakstad C, Fasmer KE, Haldorsen IS, Zaffagnini A, Häkkinen MR, Auriola S, Dubois L, Lieuwes N, Verhaegen F, Schyns LE, Kruitwagen RF; ENITEC Consortium, Xanthoulea S, Romano A. Development of an Image-Guided Orthotopic Xenograft Mouse Model of Endometrial Cancer with Controllable Estrogen Exposure. *Int J Mol Sci*. 2018 Aug 28;19(9). pii: E2547.

Versluis M, Plat A, de Bruyn M, Matias-Guiu X, Trovic J, Krakstad C, Nijman HW, Bosse T, de Bock GH, Hollema H. L1CAM expression in uterine carcinosarcoma is limited to the epithelial component and may be involved in epithelial-mesenchymal transition. *Virchows Arch*. 2018 Nov;473(5):591-598. Epub 2018 Aug 23.

Seo MK, Cairns J. Do Cancer Biomarkers Make Targeted Therapies Cost-Effective? A Systematic Review in Metastatic Colorectal Cancer (mCRC). *PLoS One*, September 26, 2018. DOI: 10.1371/journal.pone.0204496.

Kelemen LE, Earp M, Fridley BL … Berchuck A (incl. Bjorge L, Krakstad C). rs495139 in the TYMS-ENOSF1 Region and Risk of Ovarian Carcinoma of Mucinous Histology. *Int J Mol Sci*. 2018 Aug 21;19(9). pii: E2473.

Moiola CP, Lopez-Gil C, Cabrera S, Garcia A, Van Nyen T, Annibali D, Fonnes T, Vidal A, Villanueva A, Matias-Guiu X, Krakstad C, Amant F, Gil-Moreno A, Colas E. Patient-Derived Xenograft Models for Endometrial Cancer Research. *Int J Mol Sci*. 2018 Aug 17;19(8). pii: E2431. Review.

Ytre-Hauge S, Dybvik JA, Lundervold A, Salvesen ØO, Krakstad C, Fasmer KE, Werner HM, Ganeshan B, Høivik E, Bjørge L, Trovik J, Haldorsen IS. Preoperative tumor texture analysis on MRI predicts high-risk disease and reduced survival in endometrial cancer. *J Magn Reson Imaging*. 2018 Dec;48(6):1637-1647. Epub 2018 Aug 13.

O'Mara TA, Glubb DM, Amant F … Thompson DJ (incl. Krakstad C). Identification of nine new susceptibility loci for endometrial cancer. *Nat Commun*. 2018 Aug 9;9(1):3166

Gjerde C, Mustafa K, Hellem S, Rojewski M, Gjengedal H, Yassin MA, Feng X, Skaale S, Berge T, Rosen A, Shi XQ, Ahmed AB, Gjertsen BT, Schrezenmeier H, Layrolle P. Cell therapy induced regeneration of severely atrophied mandibular bone in a clinical trial. *Stem Cell Res Ther*. 2018 Aug 9;9(1):213.

Lu Y, Beeghly-Fadiel A, Wu L … Long J (incl. Bjorge L). A Transcriptome-Wide Association Study Among 97,898 Women to Identify Candidate Susceptibility Genes for Epithelial Ovarian Cancer Risk. *Cancer Res*. 2018 Sep 15;78(18):5419-5430. Epub 2018 Jul 27.

Valla M, Mjønes PG, Engstrøm MJ, Ytterhus B, Bordin DL, van Loon B, Akslen LA, Vatten LJ, Opdahl S, Bofin AM. Characterization of FGD5 Expression in Primary Breast Cancers and Lymph Node Metastases. *J Histochem Cytochem*. 2018 Nov;66(11):787-799. Epub 2018 Jul 27.

Bozickovic O, Skartveit L, Engelsen AST, Helland T, Jonsdottir K, Flågeng MH, Fenne IS, Janssen E, Lorens JB, Bjørkhaug L, Sagen JV, Mellgren G. A novel SRC-2-dependent regulation of epithelial-mesenchymal transition in breast cancer cells. *J Steroid Biochem Mol Biol*. 2019 Jan;185:57-70. Epub 2018 Jul 23.

Omsland M, Pise-Masison C, Fujikawa D, Galli V, Fenizia C, Parks RW, Gjertsen BT, Franchini G, Andresen V. Inhibition of Tunneling Nanotube (TNT) Formation and Human T-cell Leukemia Virus Type 1 (HTLV-1) Transmission by Cytarabine. *Sci Rep*. 2018 Jul 24;8(1):11118.

Kreitman RJ, Dearden C, Zinzani PL … Giles F (incl. Gjertsen BT). Moxetumomab pasudotox in relapsed/refractory hairy cell leukemia. *Leukemia*. 2018 Aug;32(8):1768-1777. Epub 2018 Jul 20.

Fonnes T, Trovik J, Edqvist PH, Fasmer KE, Marcickiewicz J, Tingulstad S, Staff AC, Bjørge L, Amant F, Haldorsen IS, Werner H, Akslen LA, Tangen IL, Krakstad C. Asparaginase-like protein 1 expression in curettage independently predicts lymph node metastasis in endometrial carcinoma: a multicentre study. *BJOG*. 2018 Dec;125(13):1695-1703. Epub 2018 Aug 19.

Earp M, Tyrer JP, Winham SJ … Phelan CM (incl. Bjorge L, Krakstad C). Variants in genes encoding small GTPases and association with epithelial ovarian cancer susceptibility. *PLoS One*. 2018 Jul 6;13(7):e0197561. eCollection 2018.

Moshina N, Sebuødegård S, Lee CI, Akslen LA, Tsuruda KM, Elmore JG, Hofvind S. Automated Volumetric Analysis of Mammographic Density in a Screening Setting: Worse Outcomes for Women with Dense Breasts. *Radiology*. 2018 Aug;288(2):343-352. Epub 2018 Jun 26.

Bischof K, Knappskog S, Stefansson I, McCormack EM, Trovik J, Werner HMJ, Woie K, Gjertsen BT, Bjorge L. High expression of the p53 isoform γ is associated with reduced progression-free survival in uterine serous carcinoma. *BMC Cancer*. 2018 Jun 25;18(1):684.

Lofterød T, Mortensen ES, Nalwoga H, Wilsgaard T, Frydenberg H, Risberg T, Eggen AE, McTiernan A, Aziz S, Wist EA, Stensvold A, Reitan JB, Akslen LA, Thune I. Impact of pre-diagnostic triglycerides and HDL-cholesterol on breast cancer recurrence and survival by breast cancer subtypes. *BMC Cancer*. 2018 Jun 15;18(1):654.

Nepstad I, Hatfield KJ, Aasebø E, Hernandez-Valladares M, Brenner AK, Bartaula-Brevik S, Berven F, Selheim F, Skavland J, Gjertsen BT, Reikvam H, Bruserud Ø. Two acute myeloid leukemia patient subsets are identified based on the constitutive PI3K-Akt-mTOR signaling of their leukemic cells; a functional, proteomic, and transcriptomic comparison. *Expert Opin Ther Targets*. 2018 Jul;22(7):639-653. Epub 2018 Jun 22.

Ladds MJGW, van Leeuwen IMM, Drummond CJ … Laín S (incl. McCormack E). Publisher Correction: A DHODH inhibitor increases p53 synthesis and enhances tumor cell killing by p53 degradation blockage. *Nat Commun*. 2018 May 22;9(1):2071.

Robsahm TE, Helsing P, Nilssen Y, Vos L, Rizvi SMH, Akslen LA, Veierød MB. High mortality due to cutaneous melanoma in Norway: a study of prognostic factors in a nationwide cancer registry. *Clin Epidemiol*. 2018 May 9;10:537-548. eCollection 2018.

Zhang B, Durán PA, Piechaczyk L, Fløisand Y, Safont MMS, Karlsen IT, Fandalyuk Z, Tadele D, Mierlo PV, Rowe AD, Robertson JM, Gjertsen BT, McCormack E, Enserink JM; Bjørn Tore Gjertsen Group; Emmet McCormack Group. GRP94 rewires and buffers the FLT3-ITD signaling network and promotes survival of acute myeloid leukemic stem cells. *Haematologica*. 2018 May 10. pii: haematol.2018.189399. [Epub ahead of print]

CCBIO 2018 - List of Publications

Jokela TA, Engelsen AST, Rybicka A, Pelissier Vatter FA, Garbe JC, Miyano M, Tiron C, Ferariu D, Akslen LA, Stampfer MR, Lorens JB, LaBarge MA. Microenvironment-Induced Non-sporadic Expression of the AXL and cKIT Receptors Are Related to Epithelial Plasticity and Drug Resistance. *Front Cell Dev Biol*. 2018 Apr 17;6:41. eCollection 2018.

Pelissier Vatter FA, Schapiro D, Chang H, Borowsky AD, Lee JK, Parvin B, Stampfer MR, LaBarge MA, Bodenmiller B, Lorens JB. High-Dimensional Phenotyping Identifies Age-Emergent Cells in Human Mammary Epithelia. *Cell Rep*. 2018 Apr 24;23(4):1205-1219.

Ladds MJGW, Pastor-Fernández A, Popova G, van Leeuwen IMM, Eng KE, Drummond CJ, Johansson L, Svensson R, Westwood NJ, McCarthy AR, Tholander F, Popa M, Lane DP, McCormack E, McInerney GM, Bhatia R, Laín S. Autophagic flux blockage by accumulation of weakly basic tenovins leads to elimination of B-Raf mutant tumour cells that survive vemurafenib. *PLoS One*. 2018 Apr 23;13(4):e0195956. eCollection 2018.

Stødle GS, Silva GB, Tangerås LH, Gierman LM, Nervik I, Dahlberg UE, Sun C, Aune MH, Thomsen LCV, Bjørge L, Iversen AC. Placental inflammation in pre-eclampsia by Nod-like receptor protein (NLRP)3 inflammasome activation in trophoblasts. *Clin Exp Immunol*. 2018 Jul;193(1):84-94. Epub 2018 Apr 23.

Wang B, Tian T, Kalland KH, Ke X, Qu Y. Targeting Wnt/β-Catenin Signaling for Cancer Immunotherapy. *Trends Pharmacol Sci*. 2018 Jul;39(7):648-658. Epub 2018 Apr 17. Review.

Ruiz de Garibay G, Mateo F, Stradella A, Valdés-Mas R, Palomero L, Serra-Musach J, Puente DA, Díaz-Navarro A, Vargas-Parra G, Tornero E, Morilla I, Farré L, Martinez-Iniesta M, Herranz C, McCormack E, Vidal A, Petit A, Soler T, Lázaro C, Puente XS, Villanueva A, Pujana MA. Tumor xenograft modeling identifies an association between TCF4 loss and breast cancer chemoresistance. *Dis Model Mech*. 2018 May 18;11(5). pii: dmm032292.

Pilskog M, Bostad L, Edelmann RJ, Akslen LA, Beisland C, Straume O. Tumour cell expression of interleukin 6 receptor α is associated with response rates in patients treated with sunitinib for metastatic clear cell renal cell carcinoma. *J Pathol Clin Res*. 2018 Apr;4(2):114-123. Epub 2018 Mar 5.

Kristoffersen AH, Petersen PH, Bjørge L, Røraas T, Sandberg S. Within-subject biological variation of activated partial thromboplastin time, prothrombin time, fibrinogen, factor VIII and von Willebrand factor in pregnant women. *Clin Chem Lab Med*. 2018 Jul 26;56(8):1297-1308.

Haaland GS, Falk RS, Lorens JB. Lower Cancer Incidence-Warfarin Effect or Immortal Time Bias? -Reply. *JAMA Intern Med*. 2018 Apr 1;178(4):585-586. No abstract available.

Painter JN, O'Mara TA, Morris AP … Spurdle AB (incl. Amant F, Krakstad C). Genetic overlap between endometriosis and endometrial cancer: evidence from cross-disease genetic correlation and GWAS meta-analyses. *Cancer Med*. 2018 May;7(5):1978-1987. Epub 2018 Apr 2.

Dixon-Suen SC, Nagle CM, Thrift AP … Webb PM (incl. Salvesen HB, Bjorge L). Adult height is associated with increased risk of ovarian cancer: a Mendelian randomisation study. *Br J Cancer*. 2018 Apr;118(8):1123-1129. Epub 2018 Mar 20.

Meregaglia M, Cairns J, Licitra L, Bossi P. The use of intensive radiological assessments in routine surveillance after treatment for head and neck cancer: an economic evaluation. *Eur J Cancer*. 2018 Apr;93:89-98. Epub 2018 Mar 20.

Ladds MJGW, van Leeuwen IMM, Drummond CJ … Laín S (incl. McCormack E). A DHODH inhibitor increases p53 synthesis and enhances tumor cell killing by p53 degradation blockage. *Nat Commun*. 2018 Mar 16;9(1):1107. Erratum in: Nat Commun. 2018 May 22;9(1):2071.

Lidén Å, Karlsen TV, Guss B, Reed RK, Rubin K. Integrin αV β3 can substitute for collagen-binding β1 -integrins *in vivo* to maintain a homeostatic interstitial fluid pressure. *Exp Physiol*. 2018 May 1;103(5):629-634.

Widschwendter M, Jones A, Evans I, Reisel D, Dillner J, Sundström K, Steyerberg EW, Vergouwe Y, Wegwarth O, Rebitschek FG, Siebert U, Sroczynski G, de Beaufort ID, Bolt I, Cibula D, Zikan M, Bjørge L, Colombo N, Harbeck N, Dudbridge F, Tasse AM, Knoppers BM, Joly Y, Teschendorff AE, Pashayan N; FORECEE (4C) Consortium. Epigenome-based cancer risk prediction: rationale, opportunities and challenges. *Nat Rev Clin Oncol*. 2018 May;15(5):292-309. Epub 2018 Feb 27. Review.

Schulz JN, Plomann M, Sengle G, Gullberg D, Krieg T, Eckes B. New developments on skin fibrosis - Essential signals emanating from the extracellular matrix for the control of myofibroblasts. *Matrix Biol*. 2018 Aug;68-69:522-532. Epub 2018 Feb 12. Review.

Lønning PE, Berge EO, Bjørnslett M, Minsaas L, Chrisanthar R, Høberg-Vetti H, Dulary C, Busato F, Bjørneklett S, Eriksen C, Kopperud R, Axcrona U, Davidson B, Bjørge L, Evans G, Howell A, Salvesen HB, Janszky I, Hveem K, Romundstad PR, Vatten LJ, Tost J, Dørum A, Knappskog S. White Blood Cell BRCA1 Promoter Methylation Status and Ovarian Cancer Risk. *Ann Intern Med*. 2018 Mar 6;168(5):326-334. Epub 2018 Jan 16.

Sønstevold T, Johannessen AC, Reed RK, Salvesen GS, Stuhr L. Hyperbaric oxygen treatment did not significantly affect radiation injury in the mandibular area of rats. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2018 Feb;125(2):112-119. Epub 2017 Nov 2.

Ludwig KF, Du W, Sorrelle NB, Wnuk-Lipinska K, Topalovski M, Toombs JE, Cruz VH, Yabuuchi S, Rajeshkumar NV, Maitra A, Lorens JB, Brekken RA. Small-Molecule Inhibition of Axl Targets Tumor Immune Suppression and Enhances Chemotherapy in Pancreatic Cancer. *Cancer Res*. 2018 Jan 1;78(1):246-255. Epub 2017 Nov 27.

Forthun RB, Aasebø E, Rasinger JD, Bedringaas SL, Berven F, Selheim F, Bruserud Ø, Gjertsen BT. Phosphoprotein DIGE profiles reflect blast differentiation, cytogenetic risk stratification, FLT3/NPM1 mutations and therapy response in acute myeloid leukaemia. *J Proteomics*. 2018 Feb 20;173:32-41. Epub 2017 Nov 21.

Halle MK, Tangen IL, Berg HF, Hoivik EA, Mauland KK, Kusonmano K, Berg A, Hurtado A, Kalland KH, Øyan AM, Stefansson I, Vintermyr OK, Werner HM, Haldorsen IS, Trovik J, Salvesen HB, Krakstad C. HER2 expression patterns in paired primary and metastatic endometrial cancer lesions. *Br J Cancer*. 2018 Feb 6;118(3):378-387. Epub 2017 Nov 23.

CCBIO 2018 - List of Publications

Konings GF, Cornel KM, Xanthoulea S, Delvoux B, Skowron MA, Kooreman L, Koskimies P, Krakstad C, Salvesen HB, van Kuijk K, Schrooders YJ, Vooijs M, Groot AJ, Bongers MY, Kruitwagen RF; ENITEC, Romano A. Blocking 17β-hydroxysteroid dehydrogenase type 1 in endometrial cancer: a potential novel endocrine therapeutic approach. *J Pathol*. 2018 Feb;244(2):203-214. Epub 2018 Jan 3.

Fasmer KE, Bjørnerud A, Ytre-Hauge S, Grüner R, Tangen IL, Werner HM, Bjørge L, Salvesen ØO, Trovik J, Krakstad C, Haldorsen IS. Preoperative quantitative dynamic contrast-enhanced MRI and diffusion-weighted imaging predict aggressive disease in endometrial cancer. *Acta Radiol*. 2018 Aug;59(8):1010-1017. Epub 2017 Nov 14.

Hugdahl E, Kalvenes MB, Mannelqvist M, Ladstein RG, Akslen LA. Prognostic impact and concordance of TERT promoter mutation and protein expression in matched primary and metastatic cutaneous melanoma. *Br J Cancer*. 2018 Jan;118(1):98-105. Epub 2017 Nov 9.

Davidenko N, Hamaia S, Bax DV, Malcor JD, Schuster CF, Gullberg D, Farndale RW, Best SM, Cameron RE. Selecting the correct cellular model for assessing of the biological response of collagen-based biomaterials. *Acta Biomater*. 2018 Jan;65:88-101. Epub 2017 Oct 26.

Fonnes T, Berg HF, Bredholt T, Edqvist PD, Sortland K, Berg A, Salvesen HB, Akslen LA, Werner HMJ, Trovik J, Tangen IL, Krakstad C. Asparaginase-like protein 1 is an independent prognostic marker in primary endometrial cancer, and is frequently lost in metastatic lesions. *Gynecol Oncol*. 2018 Jan;148(1):197-203. Epub 2017 Oct 31.

Qu Y, Olsen JR, Yuan X, Cheng PF, Levesque MP, Brokstad KA, Hoffman PS, Oyan AM, Zhang W, Kalland KH, Ke X. Small molecule promotes β-catenin citrullination and inhibits Wnt signaling in cancer. *Nat Chem Biol*. 2018 Jan;14(1):94-101. Epub 2017 Oct 30.

Taxt T, Reed RK, Pavlin T, Rygh CB, Andersen E, Jiřík R. Semi-parametric arterial input functions for quantitative dynamic contrast enhanced magnetic resonance imaging in mice. *Magn Reson Imaging*. 2018 Feb;46:10-20. Epub 2017 Oct 21.

Reisæter LAR, Fütterer JJ, Losnegård A, Nygård Y, Monssen J, Gravdal K, Halvorsen OJ, Akslen LA, Biermann M, Haukaas S, Rørvik J, Beisland C. Optimising preoperative risk stratification tools for prostate cancer using mpMRI. *Eur Radiol*. 2018 Mar;28(3):1016-1026. Epub 2017 Oct 6.

Ytre-Hauge S, Esmaeili M, Sjøbakk TE, Grüner R, Woie K, Werner HM, Krakstad C, Bjørge L, Salvesen ØO, Stefansson IM, Trovik J, Bathen TF, Haldorsen IS. *In vivo* MR spectroscopy predicts high tumor grade in endometrial cancer. *Acta Radiol*. 2018 Apr;59(4):497-505. Epub 2017 Sep 19.

Mejlgaard N, Christensen MV, Strand R, Buljan I, Carrió M, Giralt M, Griessler E, Lang A, Marušić A, Revuelta G, Rodríguez G, Saladié N, Wuketich M. Teaching Responsible Research and Innovation: A Phronetic Perspective. *Sci Eng Ethics*, 1-19, 07 February 2018.

Romaine A, Sørensen IW, Zeltz C, Lu N, Erusappan PM, Melleby AO, Zhang L, Bendiksen B, Robinson EL, Aronsen JM, Herum KM, Danielsen HE, Sjaastad I, Christensen G, Gullberg D. Overexpression of integrin α11 induces cardiac fibrosis in mice. *Acta Physiol (Oxf)*. 2018 Feb;222(2). Epub 2017 Aug 30.

Blanchard A, Strand R, (eds): Cancer Biomarkers: Ethics, Economics and Society, 2nd revised printing, Bergen, *Megaloceros Press*, 2018.

CCBIO

CAPTURING CANCER COMPLEXITY
AND CLINICAL CHALLENGES

8th CCBIO ANNUAL SYMPOSIUM MAY 12-13 2020

SOLSTRAND // BERGEN // NORWAY

Norwegian Centre of Excellence

The Research Council of Norway

Annual Symposium

23th-24th May 2018

CCBIO Investigators and Invited Speakers

Front row, from left to right: *Oddbjørn Straume, Rolf K. Reed, Roger Strand, James B. Lorens, Lars A. Akslen, Anne Christine Johannessen, Karl-Henning Kalland, Inge Jonassen, Emmet McCormack.*

Middle row, from left to right: *Jean-Paul Thiery, Richard Hynes, Camilla Krakstad, William N. William Jr., Arne Östman, Fanny A. Vatter, Jean-Christophe Bourdon, Therese Sørlie, Eirik Tranvåg, Ritva Heljasvaara, Line Bjørge, Ian G. Mills, John Cairns, Ole W. Petersen.*

Upper row, from left to right: *Hani Gabra, Leonard Fleck, Elisabeth Wik, Randolph S. Watnick, Liv C. V. Thomsen, Daniela E. Costea, Ulf Landegren, Gry S. Haaland, Hrvoje Miletic, Kenneth Finne, Thomas F. Meyer, Carina Strell, Frederic Amant, Rolf A. Brekken, Bruce R. Zetter, Ragna Breines, Mark LaBarge.*

CCBIO

ccbio.no

CCBIO

- capturing cancer complexity and clinical challenges

CCBIO
Norwegian Centre of Excellence
University of Bergen

Norwegian Centre of Excellence
The Research Council of Norway