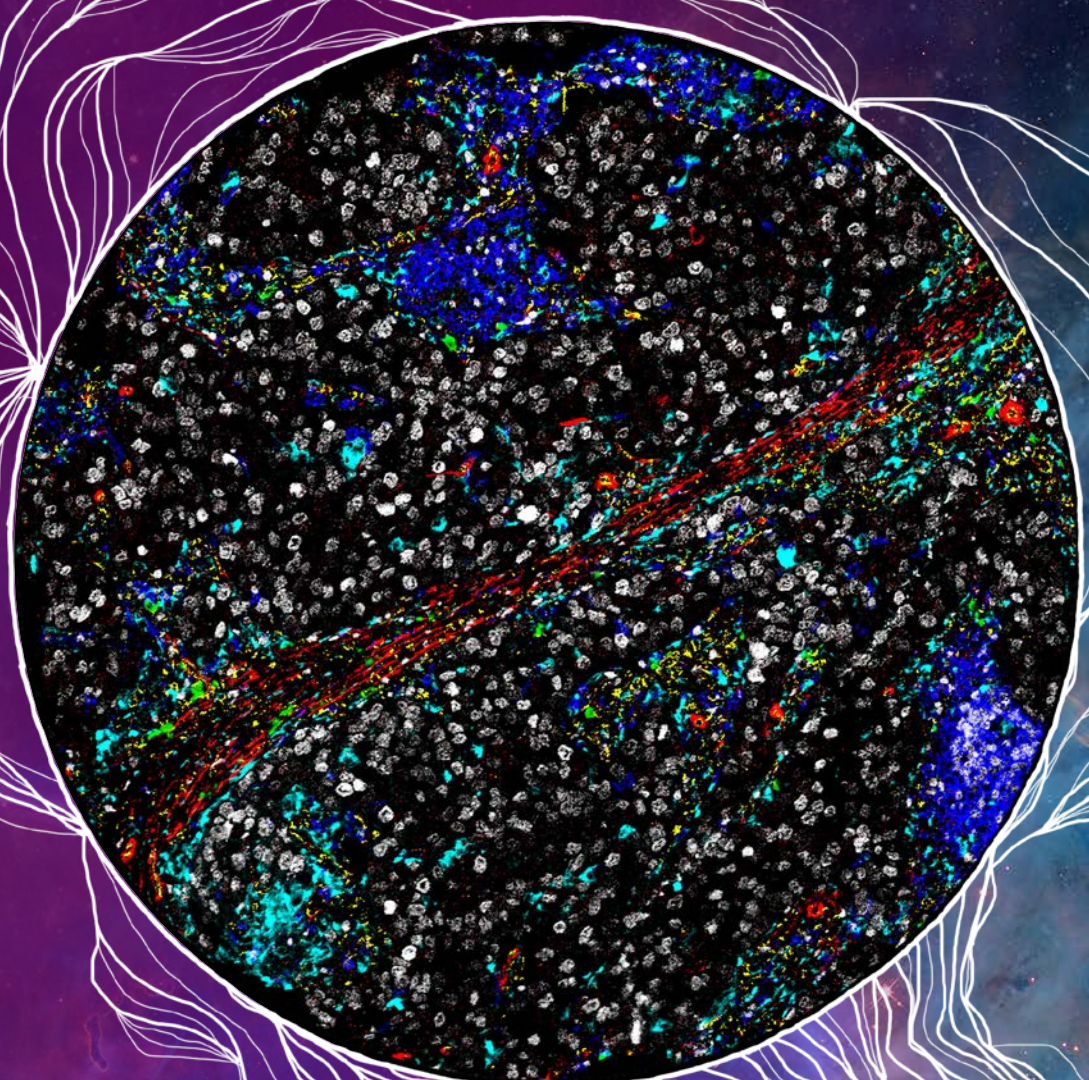
Centre for Cancer Biomarkers

Norwegian Centre of Excellence – University of Bergen

Norwegian Centre of Excellence

The Research Council of Norway



ANNUAL REPORT 2019

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CCBIO - capturing cancer complexity and clinical challenges

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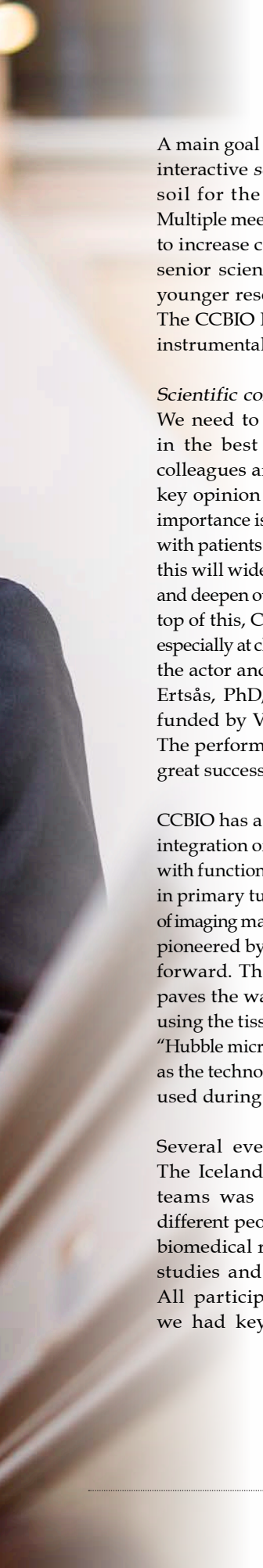
COVER PICTURE: Lars A. Akslen & Kenneth Finne (imaging mass cytometry of breast cancer)
BACK COVER: Crab Nebula (NASA)

Several of the portraits and illustration pictures are taken at the newly refurbished **Museum of Natural History** at UiB.

Director's Comments



A main goal for CCBIO is to create and maintain an interactive *scientific community* as a stimulating soil for the many scientific ideas and talents. Multiple meetings and meeting places are important to increase collaboration and networking between senior scientists and group leaders, and among younger researchers as a resource for the future. The CCBIO Research School for Cancer Studies is instrumental to achieve this.

Scientific communication is another cornerstone. We need to communicate our findings not only in the best scientific journals, but also to our colleagues and to the general public, among them key opinion leaders and politicians. Of particular importance is that we should increase our interaction with patients and their organizations. In the long run, this will widen our perspectives on "real life patients" and deepen our understanding of ultimate impact. On top of this, CCBIO has a communication effort aimed especially at children and youths in collaboration with the actor and cancer researcher Henriette Christie Ertsås, PhD, a CCBIO alumna. This program is funded by Vestland Fylkeskommune and CCBIO. The performances are interactive and have been a great success.

CCBIO has a focus on *cellular communities* and the integration of tissue landscapes and cellular location with functional properties in various "cellular niches" in primary tumors and distant tissues. The establishment of imaging mass cytometry by the Hyperion platform, pioneered by the Bodenmiller team, is clearly a step forward. This multi-dimensional tissue profiling paves the way for a systems biology interrogation using the tissue slide format. We have called this the "Hubble microscope" of contemporary tissue analysis, as the technology reminds us of the Hubble telescope used during the early days of deep space imaging.

Several events have taken place during 2019. The Iceland Research Meeting for some of our teams was memorable. We had a good mix of different people and research topics, ranging from biomedical research to societal and philosophical studies and projects on cancer communication. All participants gave short presentations, and we had keynote lectures on the "thalidomide story" in cancer treatment and on the art of "scientific saga telling" and interactive teaching. The lively discussions provided a basis for *scientific eruptions*.

Two members of our Scientific Advisory Board were honored this year. In October, Carl-Henrik Heldin, Chairman of the CCBIO SAB, received The Anders Jahre Senior Medical Prize at the University of Oslo, for his outstanding research about growth factors and cancer. Also in October, Bruce Zetter was appointed as an Honorary Doctor at the University of Bergen, for his ground-breaking studies in the fields of cancer angiogenesis and metastases, and for his unique teaching and mentoring. Congratulations to both!

Four CCBIO Opinion pieces are included in this Annual Report. Mills comments on some of the transformative forces in contemporary translational cancer research, paying special attention to big data analysis and artificial intelligence. Bremer & Wik argues that "perfect biomarkers" are extremely difficult to develop and that in many cases, "good enough biomarkers" could be efficient and advance precision management of many cancers, by balancing opportunities and limitations. Stenmarck & Nilsen discuss some of their findings related to how cancer challenges are communicated in the news, lacking in nuance and resulting in simplistic and faulty public understanding. Researchers must strive for both awareness and ownership of how their findings are presented in the public discourse. Cancer philosopher Bertolaso tells a tale about Cecil Rhodes and the diamond miners, as a metaphor for today's "big data mining", and she reminds us of the necessity of complex data integration to improve our conceptual understanding of the tumor systems.

At this point, it is not easy to measure the impact of our activities. In the meantime, we do our best to communicate interim outcomes in our fields. As a long-term strategy, we constantly feel an obligation to motivate our young recruits for a rewarding career in the "diamond mines" of cancer research. ••

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 tumor 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 behavior. The center is studying how crosstalk between tumor cells and components in the tumor microenvironment reflects 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 integrated programs:

1. Mechanisms of Tumor-Microenvironment Interactions (Basic Studies)

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

3. Clinical Applications and Early Trials (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. Collaboration partners, both national and international, have been included to support these programs. ••

CCBIO Opinion
Text: Ian Mills, CCBIO

Transformative Forces in Translational Cancer Research

It is a truism that translational cancer research has and always will be subject to transformative forces. However technological advances and societal expectations have made us - as researchers, clinicians and citizens - far more aware of these over the last two decades. Where do we stand today and what is the role of CCBIO in shaping these forces and these expectations? The ability to generate 'Big Data', be that sequencing data or imaging data or indeed to interrogate clinical data, has created arguably the greatest excitement in translational cancer research. The promise is that more data will allow disease to be more precisely classified, the underlying drivers of cancer to be identified and the most effective treatments to be administered to the right patients at the right time. The scale of the molecular data that we are generating is increasing all the time and can increasingly be mapped to smaller units within cancers – at the resolution of single cells in many cases. The race for data has undoubtedly catalyzed rapid innovation and reductions in the costs of generating such data per patient – manifested most clearly in the cancer genomics space. In and of itself, 'Big Data' will not have a translational impact until it can be generated in real time/over short time periods and be readily accessed and interrogated to inform clinical decision making. Traditional clinical pathology is of course very effective in informing clinical decisions in short timeframes, based often on visual evaluations of tissue samples or stains for individual markers. The recent focus on artificial intelligence and machine learning approaches in cancer research is an attempt to align 'Big Data'/multi-parametric measurements with an analytical framework that can deliver disease stratification or treatment selection for patients in short timeframes.

One example of this, is the recent adoption of multi-parametric magnetic resonance imaging (mpMRI) to guide prostate cancer biopsy. This has led to a fundamental shift in the pathological grading of biopsies downstream and an enrichment for intermediate- and high-Gleason Grade Group disease. This in turn provide clinicians with greater certainty in making risk assessments and consenting patients for treatment and monitoring. As a result, in Europe, mpMRI-guided biopsy has been incorporated into the European Association of Urology's clinical guidelines for prostate cancer detection. This in turn has spurned a heightened interest in radiomics and the possibility of further refining the interpretation of mpMRI and risk stratification of prostate cancer patients based on pairing imaging data with molecular information generated from the subsequent biopsy samples.

Imaging is of course only one example of a transformative force in translational cancer research. Another is the development of portable medical devices able to make affordable, rapid and sensitive real-time biomarker measurements. Esophageal cancer provides two interesting examples of this at opposite ends of the technology spectrum. At the low-cost end there is the 'cyto-sponge'. This is a capsule on a string which when swallowed expands into a sponge which can then be fished out through the esophagus using a string and in so doing collects cytological samples from the wall of the esophagus. The material collected has been used successfully to support biomarker detection predictive of Barrett's esophagus, a precursor for esophageal cancer. At the other end of the spectrum is a hand-held breathalyzer containing sensors that permit the detection of metabolites associated with heightened risk of esophageal cancer. As affordable and minimally invasive devices become accessible for monitoring and early cancer detection, the promise is that survival rates will improve because monitoring and interventions will happen before cancers disseminate or reach end stages.

In order to develop any of these approaches and maximize their impact, there needs to be a step change in how academia, industry and government interact. In the loosest sense, this step change requires all of these entities to communicate effectively and share data and innovations. To support this, we need spaces (physical and virtual) in which these interactions can happen, which are multi-disciplinary and multi-stakeholder and encourage people to take risks and experiment. CCBIO is a multi-disciplinary environment within which all of these stakeholders are present and active. The future of translational cancer research requires initiatives like this to be scaled up even further. To do so requires a society with a strong and stable capital base (both human and financial) and high degree of openness and mutual respect across sectors and disciplines. It also requires a society which naturally takes a long-term view and makes long-term commitments. Norway's approach to its energy sector and the resultant capital accrued from that approach exemplifies this. I have no doubt that CCBIO and Norway will be transformative forces in translational cancer research if the will exists to transpose those principles into biomedical research on a large scale. ••

CCBIO Opinion

Text: Anne Bremer & Elisabeth Wik, CCBIO

"Good Enough" Biomarkers in a Centre of Excellence?

Hope, enthusiasm, and the search for perfection

Much hope and enthusiasm is placed in precision oncology, which many imagine as the ideal future of medical science. Precision oncology is expected to "help anticipate and cure illnesses" by delivering "tailored and optimized health prevention, diagnosis, and treatment" (EC, 2019), resulting in more sustainable health care systems through a fairer and more effective allocation of resources. Precision oncology relies on having biomarkers that are accurate, precise, sensitive, specific, safe and relatively easy to use in clinical practice. In other words, "perfect biomarkers". This is a lot to ask for, especially considering the high levels of biological complexity and uncertainty we are faced with. We therefore argue that it is important to also think in terms of "good enough" biomarkers (Blanchard & Wik, 2017). Yes, even in a Centre of Excellence!

What is a "good enough" biomarker?

Thinking in terms of "good enough" biomarkers means critically thinking about what precision medicine can and cannot bring. It is about balancing opportunities and limitations: a biomarker, no matter how sophisticated, can't bring all the answers or solutions. Biomarkers have a particular purpose, which will exclude other purposes or qualities. For instance, a biomarker cannot be highly precise and complex while also being accessible to all, nationally or globally. The more sophisticated a biomarker becomes, the more stringent challenges of quality and validation it will face, and the more difficult it will be to implement it in clinical practice.

Thinking about "good enough" biomarkers also means accepting the fact that even the best biomarker will never match the biological and social complexity of cancer. No matter how sophisticated a biomarker is, we will still be left with ethical dilemmas and questions of the "common good". Wherever we place the cut-off for patient stratification, some patients will suffer.

The need to reintroduce meaning in precision oncology research

Thinking about "good enough" biomarkers is stepping back from the workbench and considering what precision oncology actually means for clinicians and patients now. Perhaps the most important biomarkers are those that offer some support to clinical decision-making, even if they are not scientifically ground-breaking. Over the last two decades, there has been a tremendous increase in the generation of "omics" data (genomics, transcriptomics, proteomics, epigenomics, etc.), with the expectations that key answers and game-changing biomarkers are hidden in these big data. But do we know how to use these data in the most meaningful ways? Trying to decipher parts of the tumor biology is interesting, but we have to ask ourselves why this is important, how exactly this might benefit society, while accounting for unforeseen challenges. What is the context within which biomarkers are used, and what should their criteria of success be? Often, the focus is on adding years to a patient's life. Adding life and meaning to those years is nevertheless equally, if not more, important.

It is also important to publicly talk about biomarkers as "good enough" tools, not as final "solutions" to prognostication and treatment selection. If we look at current discourses in the media, in politics or by patients' advocacy groups, it sounds like precision medicine for all is just around the corner. Individuals now expect long and healthy lives and claim the right to have access to extraordinary treatments. Managing expectations in the public sphere starts by managing expectations in the lab and research environments. Arguably, part of what makes CCBIO excellent, is that it is nurturing these kinds of discussions about being good enough and meaningful. ••

Blanchard, A., & Wik, E. (2017). What is a good (enough) cancer biomarker? In A. Blanchard & R. Strand (Eds.), Cancer Biomarkers: Ethics, Economics and Society (pp. 7-24). Kokstad, Norway: Megaloceros Press.

Vincente, A. M., Ballensiefen, W., Donertas, D., Eklund, M., Ivask, A., Jönsson, J.-I., et al. (2019). The ICPerMed vision for 2030: How can personalised approaches pave the way to Next-Generation Medicine? EU ICPerMed.

CCBIO Opinion

Text: Mille S Stenmarck & Irmelin W Nilsen, CCBIO

Cancer in the News

The issue of cancer and cancer drugs holds a considerable presence in the Norwegian media. The public interest in the issue has been especially persistent in recent years with the rise and alleged promise of precision medicine. Though cancer treatment becomes more personalized and, sometimes, more effective, increasingly many lives are lost to the illness as populations age and become more prone to cancer disease. Simultaneously, increasing amounts of public health budgets are devoted to cancer treatment, and the ensuing priority-setting dilemmas both engage and provoke within the general public. In the news, the issue of cancer and cancer drugs is thus cloaked in controversy, within a public discourse that heavily emphasizes the tragic choices aspect of this issue.

An analysis of over 500 Norwegian newspaper articles on the issue of cancer and cancer drugs identified four premises which seemingly underlie the entire discourse: (1) cancer drugs are de facto expensive and we need not question why; (2) these drugs work, and there is no need to question their efficacy; (3) any health benefit for a cancer patient is an absolute good; whatever time can be won is a blessing, and there is no need to consider what shape that time will have; (4) patients and doctors own the truth about cancer and cancer drugs, and "outsider" perspectives are superfluous. A separate study on how cancer research is presented in the news by actors within the field of cancer, as well as by journalists, proved that the framings are strongly influenced by what the actors themselves imagine to be a good and attainable future of cancer treatment. These visions, however, seem to be characterized by normative understandings of what the future should hold. Three main future visions proved prominent: (1) personalized medicine will revolutionize cancer treatment, (2) artificial intelligence will make diagnosis and treatment more efficient, and (3) cancer is Norway's next billion-dollar industry.

Our studies on the framing of cancer and cancer research in the news

suggest that the storytelling on cancer is considerably lacking in nuance. The adherence to the above-mentioned premises arguably contributes to false understandings both of what cancer research and new cancer treatments are, and of the promise they hold. This serves to increase the current discrepancy between public expectations, medical possibilities and financial constraints. Further, these framings do not devote adequate attention to the ethical and societal challenges that may arise from researchers' own unambiguously positive presentations of the future of cancer treatment. Overall, the framing of the issue seems to be derived from two fundamental assumptions; (1) that contemporary cancer treatment is and must be an issue of tragic choices, within a healthcare system of winners and losers – between patients who gain access to new and expensive treatments, and those who are denied it. And (2) that cancer research and the future of cancer treatment remains an indubitable oasis of hope, with socio-technological imaginaries swarming with promise as a panacea for the tragedy that is cancer.

The general public's understanding of scientific progress – both its promise and its limits – on the issue of cancer and cancer drugs, is determined largely by its presentation in the news. In the current media climate, the framing of cancer stems from the above-mentioned premises as well as scientists' own future visions, and is subsequently compounded by a deterministic and unnuanced journalistic presentation. This results in simplistic and faulty public understandings of the issue as a whole. It should be a central objective to researchers that their work is portrayed accurately and accountably in the media, and in a manner which provides the general public with an understanding of the real value of that research. In order to achieve this, researchers must strive for both awareness as well as ownership of how their findings are presented in the public discourse, and of flaws in this presentation. ••

CCBIO Opinion

Text: Marta Bertolaso, CCBIO

South African Diamond Miners One Hundred Years Ago and Laboratory Researchers (or Biologists) Today

At the end of the nineteenth century, the young English businessman Cecil Rhodes hired thousands of South African youths to dig diamond mines. These very hard-working young Africans dug a "deluge of diamonds". In just a few decades, Cecil Rhodes became one of the richest men in the world, England became one of the richest countries in the West, and the West became the richest part of the world.

South Africans continued to dig diamonds without understanding the real meaning of their work and without grasping the laws of finance and the power mechanisms of Western countries. For this reason, all these young diamond diggers died poor and worn-out.

I find similarities between these diamond diggers and today's young laboratory researchers, "digging" a "deluge of data" in the fields of genomics, proteomics, metabolomics, etc., but for what purpose? "They're fundamental for medical science" someone might say, just as young South Africans used to say: "Diamonds are fundamental for English people". But what is this science?

The South African diggers failed to shift from the linear concept of "digging for money" to the general idea of the system of finance. Laboratory biologists are still struggling to shift from the concept of linear causation ("the billiard ball model") toward a systemic view of biological processes.

The complexity of biological processes is pushing scientists to rethink the concept of causation, primarily by considering not only the components of the systems but also their relationship and their evolution over time. This explains, for example, the methodological and epistemic relevance of the microenvironment. However, rethinking the concept of causation does not exclude the possibility of reformulating the original question that pushes researchers to "dig" for specific data.

In this "search for a meaning", philosophers are leading the scientific community to re-integrate epistemological and theoretical questions into the technological advancement of research. Without a meaning, diamonds were only stones under the soil for the South African diggers. Without a meaning, data are lists of insignificant information and their extraction a meaningless "mechanical' task in the daily life for researchers.

Rhodes was neither rich nor a genius at the beginning of his carrier. He was simply a young, sick boy sent to breathe clean, fresh air in South Africa. His only quality was the ability to observe and make connections. This story can be an example of how science can advance even without a huge budget.

By analogy with the experience of the South African diamond diggers, we can ask these questions about our own work as laboratory scientists: How do we integrate ourselves with our work? How should young scientists be educated? What skills do we really need? What is the system we are working for … and to what end? ••

Sometimes it looks like we laboratory researchers in such fields as genomics, proteomics, and metabolomics are working to sustain academical and pharmaceutical systems, forgetting that we are working to heal people. ••

Mitchel SD (2009) Unsimple Truths, Science, Complexity and Policy. The University of Chicago Press.

Bertolaso M (2016) Philosophy of Cancer – A Dynamic and Relational View. Springer Series in "History, Philosophy and Theory of the Life Sciences"

Organization of the Center

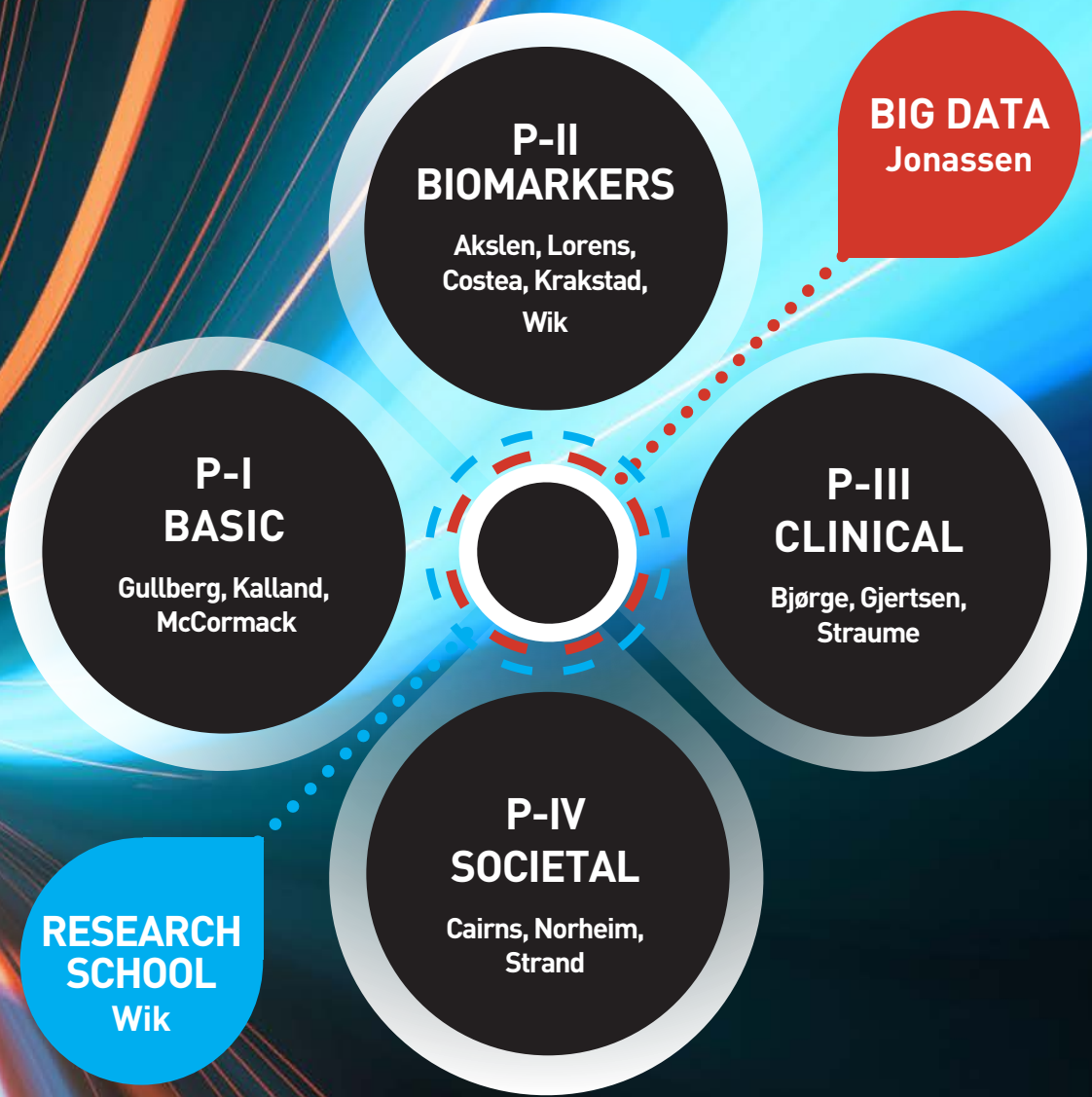
CCBIO is organized across seven departments and four faculties at the University of Bergen. Its main activities, with PIs, AIs, and most of the other staff, are located at the Faculty of Medicine's departments: The Department of Clinical Medicine, the Department of Clinical Science, and the Department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

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.

Lab space and advanced core facilities are available for CCBIO, as is the Clinical Trials Unit at Haukeland University Hospital. The investigators meet monthly to discuss scientific and administrative issues and update each other on development and progress, and they also gather for a lunch-to-lunch strategy seminar bi-annually. The monthly meetings and the bi-annual strategy seminars are important platforms for communication and ever-increasing cohesion and collaboration within CCBIO.

Management group
In 2019, CCBIO was managed by the director, Professor Lars A. Akslen, the co-director, Professor Bjørn Tore Gjertsen, and the administrative leader, Geir Olav Løken. The management is advised by a strategic advisor, Rolf K. Reed, and is assisted by a web and newsletter editor, a research advisor, four finance officers, 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. ••



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

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 investigators, mostly in connection with the CCBIO Annual Symposium. The feedback from the SAB 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 previous recommendations.

In their 2019 report, the SAB stated that they were impressed by the progress made during the last year. CCBIO has developed into a strong center that is driving biomolecular marker research in Norway. Given the success of CCBIO, the SAB encourages the University of Bergen to provide appropriate economic support to ensure that the momentum which CCBIO has built up in biomarker research can be taken care of after 2023.

The SAB noted particular strength in translating basic data into clinical studies and ongoing trials. CCBIO was recommended to focus on clinical trials, on usefulness of either biomarkers that have been derived from basic research performed within CCBIO or biomarkers from the current literature.

The SAB also commented that a noticeable team spirit has been built, which enhances the performance of individual investigators. Given the quality of the work performed at CCBIO, the SAB encourages even greater risk taking in approaching scientific and clinical problems that are currently understudied, such as the use of biomarkers in predicting the best use of therapeutic combinations, or in predicting unexpected toxicities. The recent acquisition of capacity for imaging mass cytometry, enabling the analysis of multiple biomarkers for the development of new signatures for a variety of clinical applications, should give additional impetus to CCBIO's efforts.

The SAB appreciates that the development and application of new biomarkers in clinical practice depends on economic determinants as much as it does on scientific quality and clinical need. The incorporation of ethics and economics into the curriculum, into the annual symposium and into the everyday workings of CCBIO, is therefore one of its great strengths.

The SAB commended the extensive effort of the CCBIO Research School for Cancer Studies towards providing education for PhD and master students as it helps to foster the new generation of biomarker researchers. In 2019, the activities established in interaction with the Vascular Biology Program at Boston Children's Hospital contributed significantly in this respect. ••

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 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.

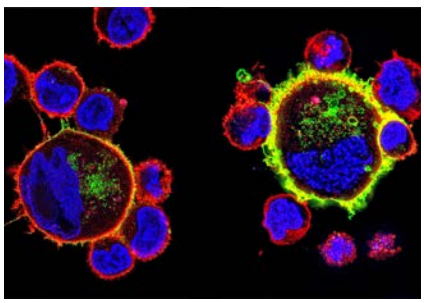
Scientific Activities and Progress 2019

CCBIO has a two-armed portfolio of biomedical (Team I-III) and societal (Team IV) projects. The Centre has a focus on biomarkers of tumor-microenvironment interactions in primary and metastatic cancers, including the expanding field of tumor immune biology, and how these properties can define aggressive tumor phenotypes and predict tumor progression and treatment response. Studies on ethics and economics represent an integrated part of CCBIO. All activities are performed in a context of interactive education and communication efforts.

During 2019, the **CCBIO Research School for Cancer Studies** has increased its activities. In addition to the basic course curriculum CCBIO901-906, a new course, CCBIO907 – Cancer Related Vascular Biology, was run and funded by INTPART. This is a collaboration with the Vascular Biology Program at Boston Children's Hospital and Harvard Medical School, with visiting faculty to Bergen. A new course, Clinical Trials in Cancer Research, with integrated Good Clinical Practice certification was introduced. The very successful two-days' Scientific Writing Seminar was repeated in 2019.

In **TEAM I**, projects are focusing on how tumor cells interact with and instruct the surrounding microenvironment, by influencing angiogenesis, cancer associated fibroblasts, immune cell participation, and matrix involvement, favoring tumor growth and metastatic spread, and explaining development of treatment resistance.

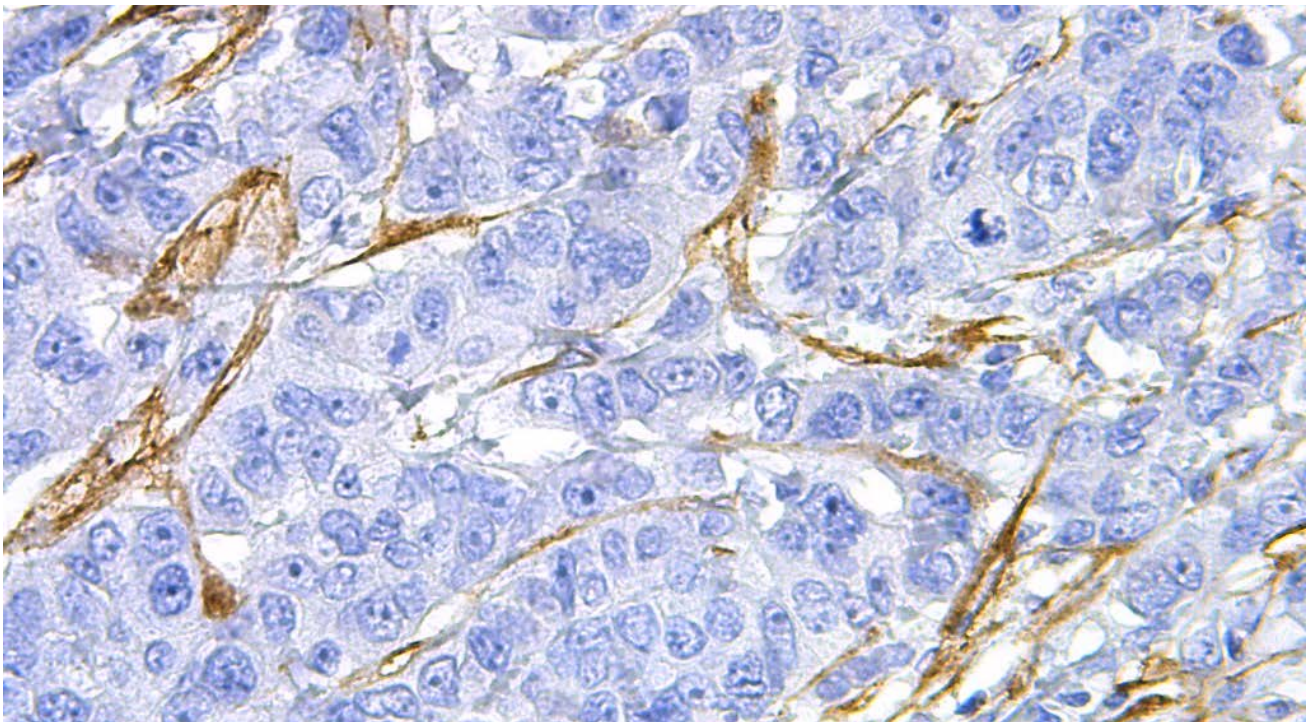
The **Gullberg group** has been working on



fibroblast biology and the characterization of novel integrin α11 function blocking antibodies and development of a mouse model to explore the role of α11 in tumor stroma. In 2019, the group reported an interaction between α11 and PDGFR-beta and the importance in breast cancer progression (*Primac et al., J Clin Invest 2019*).

In the **Kalland group**, focus has been on two strategies: drug discovery and development by repurposing, and the concept of cryo-immunotherapy (CryoIT). Some of the screened drugs have been shown to inhibit either β-catenin or STAT3 signaling. These are important regulators of tumor-initiating prostate cancer cells. During 2019, a phase I clinical trial for CryoIT for patients with advanced prostate cancer was completed. Treatment effects were suggested according to radiology, circulating tumor cell enumeration, large-scale serum auto-antibody profiling and ultradeep T-cell receptor sequencing, and the results are prepared for submission.

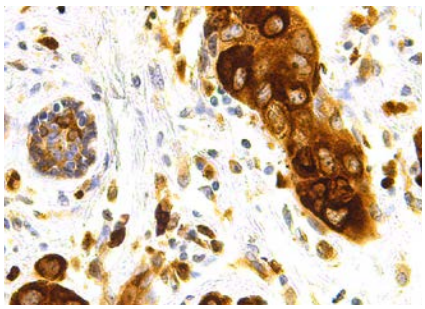
The **McCormack group** has had a major focus on the importance of studying appropriate preclinical models (organoids, PDX) before clinical trials are performed. Such models have been developed and explored for gynecologic cancers, leukemias, pancreatic cancers, and others. Several imaging techniques have been studied, for example against CD24 in high-grade ovarian cancers in PDX-models, aiming for increased sensitivity in tumor detection and more precise surgery. Strategies for improved drug delivery have been examined, for example by using sonoporation, showing how this might impact the intracellular signaling of cancer cells with



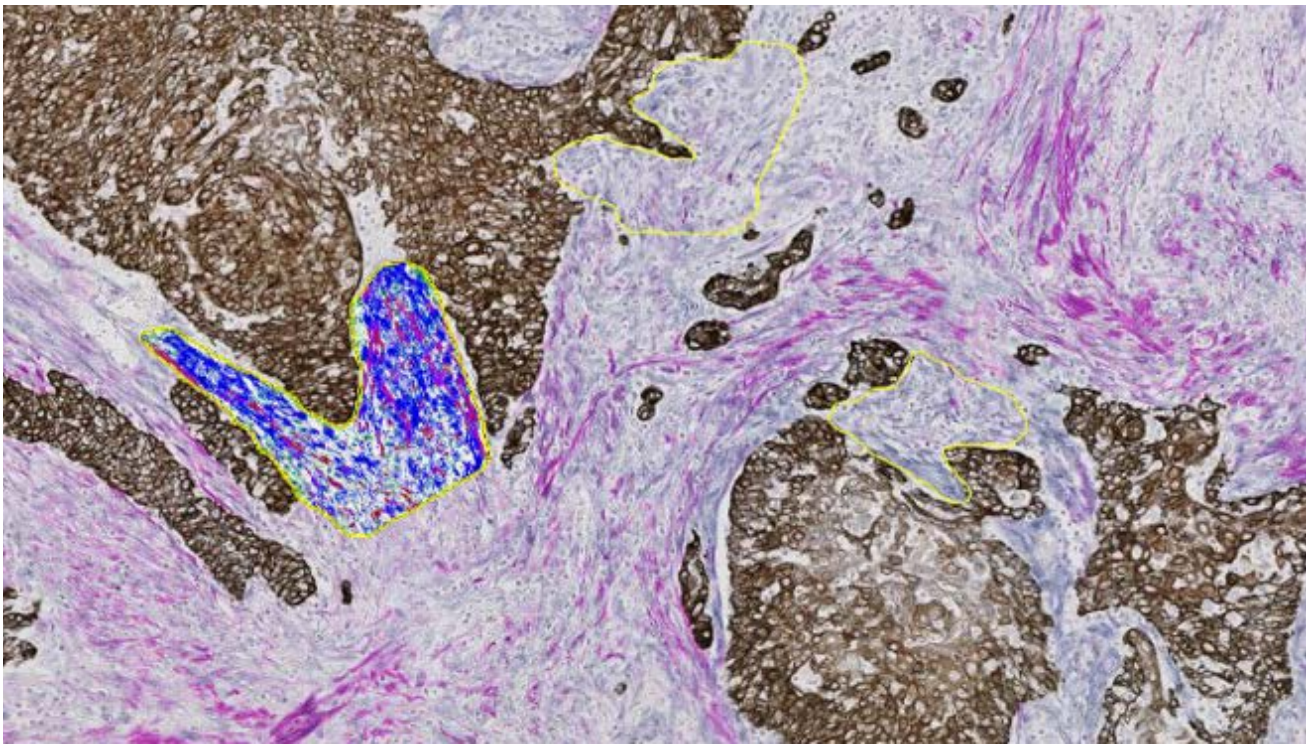
identification of biomarkers (*Haugse et al., Pharmaceutics 2019*).

In **TEAM II**, studies are being performed on biomarker discovery and validation in several tumor types, with additional work on how such markers are related to underlying mechanisms for tumor progress, tumor immune responses, and development of resistance to various treatments. Efforts are made to map tumor diversity and associations with clinico-pathologic phenotypes and patient outcome.

The **Akslen group** concentrates on tissue-based biomarkers for better molecular grading of malignant tumors and improved prediction of prognosis and treatment response. The main focus is now on proteomics profiling of luminal-like and basal-like breast cancers, with particular attention to hypoxia responses and metabolic differences as well as markers for a neuro-angiogenic phenotype in aggressive tumors. Here, laser captured micro-dissected samples of the tumor cell and microenvironment compartments are studied separately. Imaging mass cytometry (IMC) is used to map the breast cancer tissue landscapes for high-order co-expression patterns with particular focus on vascular and immune cell components. In addition, markers such as Nestin and Stathmin are studied in more detail. During 2019, a report on tissue structure by radiologic analysis of breast cancers was presented (*Hofvind et al., Lancet Oncol 2019*).

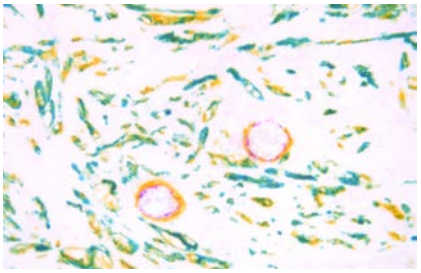


The **Lorens group** has been studying various aspects of how the Axl receptor tyrosine kinase is involved as a key regulator of normal adult epithelial progenitor cells and a determinant of carcinoma cell plasticity and interactions at the tumor-immune interface. The results have shown an important role of Axl in epithelial-mesenchymal transition (EMT) and immune evasion. Mechanisms of acquired resistance to targeted treatment in malignant tumors have been uncovered, and studies have demonstrated how anti-Axl treatment (by bemcentinib) can reverse these processes. In one project, Axl inhibition drove tumor cell differentiation and reversed gemcitabine resistance and potentiated an immune stimulatory microenvironment by targeting immune suppressive myeloid cell types. Thus, Axl targeting affects pathways that improve treatment efficacy. During 2019, the group showed that Axl is a key factor in acquired resistance to EGFR targeted treatment in lung cancer (*Lotsberg et al., J Thor Onc 2019*). Lorens and his team focus on high-dimensional single cell studies using the established imaging mass cytometry plat-



form. Axl immunohistochemistry is being developed in collaboration with BerGenBio as a companion diagnostic test for bemcentinib treatment.

The **Costea group** studies tumor-stroma interactions in oral and vulvar squamous carcinoma, with particular focus on metabolic reprogramming of



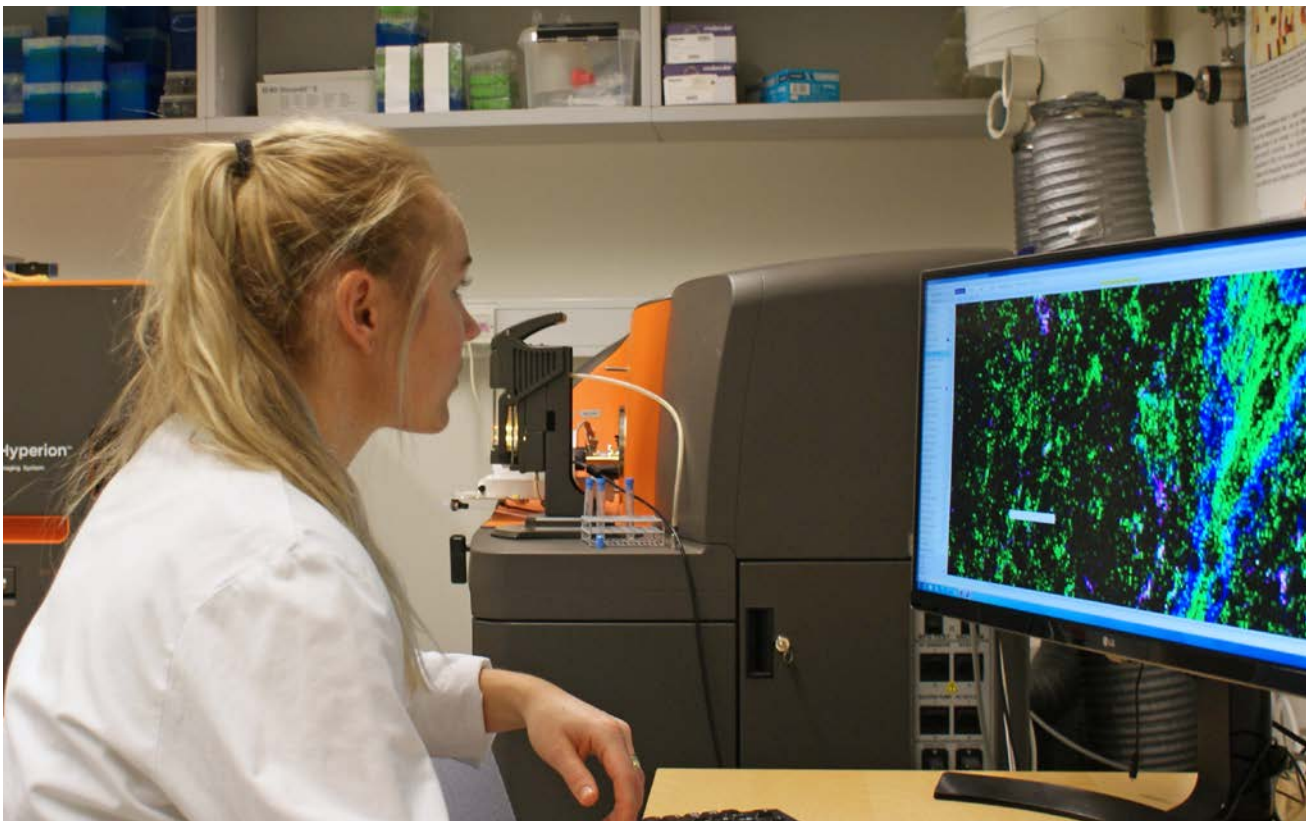
carcinoma associated fibroblasts (CAFs), and the association with genetic alterations, including HPV subtypes and their role for tumor progression. The group previously demonstrated transcriptional heterogeneity among CAFs. During 2019, the group showed how a novel metabolic coupling between oral carcinoma cells and normal neighboring fibroblasts are induced to export mitochondria towards carcinoma cells through direct contact or indirect mechanisms (*Zhang et al., Cell Mol Life Sci. 2019*).

In studies of gynecologic cancers by the **Krakstad group**, tissue and serum-based biomarkers have been further explored, with special focus on estrogen regulated pathways and their prognostic value. The international MOMATEC2 study (NCT02543710), a phase 4 implementation trial for validation of ER/PR status to stratify for lymphadenectomy in endometrial cancer, is ongoing and co-ordinated by the group. Novel PDX models for endometrial cancer have been established, and integration of molecular and radiologic data with clinical phenotypes is ongoing. During 2019, the group reported that PIK3CA amplification is associated with aggressive phenotypes but not markers of AKT-mTOR signaling in endometrial cancer (*Holst et al., Clin Cancer Res 2019*).

The **Wik group** has a focus on breast cancer of the young and why these patients often experience a more aggressive disease behavior. A large cohort has been established with multiple molecular and clinico-pathologic annotations, including primary tumors and metastases, and further genetic and imaging mass cytometric profiling is ongoing. So far, studies have been performed on estrogen related signaling networks and transcriptomic profiles with particular attention to aggressive patient subgroups.

In **TEAM III**, the main focus is to perform clinical trials with associated biomarker studies, and to promote novel findings on markers and treatments for clinical implementation and change of practice.

The **Gjertsen group** has been focusing on single cell biomarker profiling of leukemia and solid cancer cells and immune cells following treatment with novel targeted therapy or conventional drugs in a trial setting, to stratify between responders and non-responders. The group has reported how single cell analysis can be used to monitor early responses in AML. In a



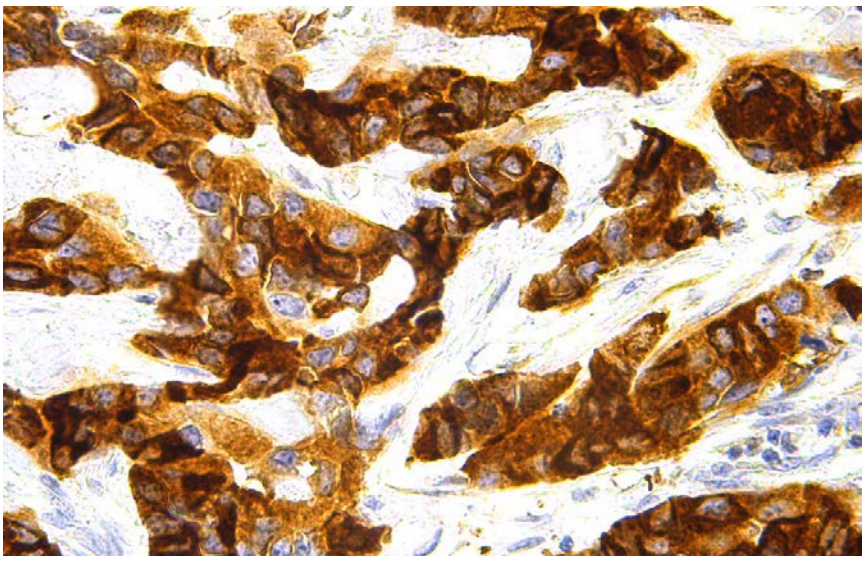
new project, the CSF1R signaling system in stromal cells is studied, and inhibition of CSF1R may represent a novel resistance mechanism. The group is also active in the p53 field, with particular attention to the importance of p53 isoforms. During 2019, the team presented results on multiparametric single cell evaluation related to drug responses in hematological cells (*Majumder et al., Haematologica 2019*).

The **Straume group** is focusing on tissue biomarker studies in clinical trials. The group has also reported the association between surgical tissue trauma and recurrence dynamics in high risk breast cancer patients. A national academic trial combining anti-Axl treatment with immunotherapy is ongoing in patients with advanced melanoma, aiming to analyze efficacy and identify potential predictive markers. A national interventional study of patients with aggressive melanoma (IPI4; ipilimumab) is also being analyzed. During 2019, the group reported a relationship between circulating tumor DNA and response to bevacizumab monotherapy in patients with malignant melanoma (*Forthun et al., Sci Rep 2019*).

The **Bjørge group** is engaged in novel multicenter trials with translational research programs related to high-grade ovarian cancer. The group also has a focus on improved imaging guided cytoreduction surgery in this disease. In addition to clinical studies, PDX models and organoid cultures are being established. High-dimensional tissue profiling of ovarian cancer samples have been initiated with special attention to immune responses. During 2019, Bjørge and colleagues reported a proof-of concept study of niraparib-bevacizumab combination therapy against niraparib monotherapy in recurrent platinum-sensitive ovarian cancer (*Mirza et al., Lancet Oncol 2019*).

In **TEAM IV**, the projects on ethics and economics of biomarker-based therapy are expanding and are being integrated in clinical trials. As CCBIO performs research on cancer biomarkers along the entire chain from studies of biological mechanism to clinical projects, the 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 management, whereas it cannot be precisely measured in the short-term. Better knowledge of cancer biomarkers is likely to affect the prioritization dilemmas, although the nature of that effect depends on the nature of the knowledge to be discovered.

CCBIO integrates work on societal perspectives and has established a team structure led by **Strand** to improve



interdisciplinary humanities and social science programs to study the opportunities and challenges of precision cancer medicine. The team will continue their collaborations on the more conceptual research into RRI and the coproduction of science, technology and society.

The **Strand group** contributes to intellectual understanding and awareness within the Centre. A key insight is that the quality of a biomarker is a complex issue with scientific and technical but also clinical, economic, ethical and political dimensions. Collaboration has increased with CCBIO ethicists (**Norheim group**) and economists (**Cairns group**). Work on a second book project is ongoing (Bremer & Strand, eds: *Precision Oncology: Issues at Stake and Matters of Concern*. The team is responsible for the basic course CCBIO903 – Cancer Research: Ethical, Economic and Social Aspects.

The main health economic projects performed by the **Cairns group** are the PhD projects 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, and 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.

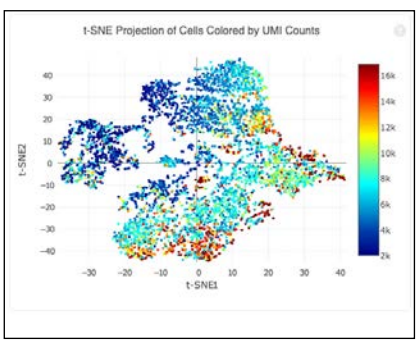
During 2019, a new PhD project has been undertaken by Jiyeon Kang (improving economic evaluation and decision-making for oncology drugs using real-world data). A paper on the cost-effectiveness profile of HSP27 in response prediction for bevacizumab in advanced melanoma was published (*Seo et al., Pharmacoecon Open 2019*).

In the **Norheim group**, an aim has been to map how cancer biomarkers can inform and hopefully improve health care priority setting, in addition to factors such as patient age. The group's findings suggest that age is widely used, directly or indirectly, to guide clinical decisions (published in 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. During 2019, the Global Health Priorities Research Group directed by Ole Frithjof Norheim has grown and developed into a center - the Bergen Centre for Ethics and Priority Setting (BCEPS), with funding from the Bill & Melinda Gates Foundation among others.

Altogether in **TEAMS I-IV**, a range of projects have been conducted and reported on since 2013. In addition, multiple new initiatives have been conceived, in part based on increasing intramural collaboration. In addition to many publications and two books presented by CCBIO, several educational activities are being performed, and we continue to reflect on the core concept and integrated activities in CCBIO and the transition to real life impact.

In addition to the activities in these teams, the **Jonassen group** has been actively collaborating across different groups on the systems biology features of many projects and processing of big data. During 2019, his team initiated a new ERAPerMed project, AML_PM - Improved Treatment of Acute Myeloid Leukemia, with partners including Gjertsen from CCBIO and Ursula Klingmüller (recruited



to the CCBIO International Faculty) and others. Postdoc Dimitrios Kleftogiannis, linked to this project, is also using part of his time to work with the Akslen and Wik groups in CCBIO. Within the AML_PM project, the group will analyze single-cell data together with gene and protein expression information and develop machine learning based approaches to predict drug responses and aid in personalized treatment of leukemia. ••

Societal Impact – Real and Imagined?

In the CCBIO Annual Report 2018, we reflected upon Sivertsen and Meijer's (2018) distinction between *normal* and *extraordinary* impact. They defined normal impact as "more-or-less active, productive and responsible interactions between (units of) research organizations according to their purposes and aims in society". "Extraordinary impact", on the other hand, are occasions of immediate and/or widespread implications for society: A revolutionary "cure"; an unusual finding with the "wow" factor. We agreed with Sivertsen and Meijer that serious research institutions should plan and work for continuous normal impact, and that the emphasis on extraordinary impact is not useful.

In the meantime, our sponsor, the Research Council of Norway (RCN), initiated an exercise to evaluate their center-of-excellence (SFF) funding program, which included requests for impact cases from the centers. We are excited to see if the RCN will be able to assess the impact of the SFF program through selected stories of impact from the centers, in ways that acknowledge the primacy of normal impact.

Reality and imagination are two important dimensions in this regard. Impacts are conventionally understood as long-term or indirect effects of outcomes; outcomes are effects of outputs. CCBIO produces outputs such as new knowledge (in the forms of research papers and human capital) but also new (clinical and research) practice. New collaborations in the *triple helix of academia, industry and public healthcare institutions* are also outputs of CCBIO, as are our diverse range of communication activities. The real outcomes of these outputs – in terms of their direct effects on researchers, clinicians and other actors – can to some extent be traced in terms of e.g. citations and changes in practice. The volume of our research outputs has been steadily increasing since we started in 2013. However, it is still too early to measure outcome; and as for the impacts, the long-term, indirect effects of the outcomes, more time is obviously needed for these to be reliably estimated.

In the field of cancer research, which receives sustained and unusually high attention in the public and in the mass media, impact is entangled with imagination. On one hand, the media is sometimes seen to report imagined extraordinary impact as real (Nilsen 2019), relaying promises that ultimately may not deliver. On the other hand, according to the famous Thomas Theorem in social science, "If men define situations as real, they are real in their consequences." Imaginations are also outputs in their own right, creating real social and political effects in society such as optimism, hope and sustained support for cancer research. The challenge for us who have committed to an ideal of Responsible Cancer Research (Strand and Akslen 2017) is to sustain realistic optimism and not contribute to beliefs in Holy Grails or other quick fixes for cancer. In a rare achievement combing biomedical research and philosophy of science, a recent CCBIO doctoral dissertation contributed to the clarification and assessment of the realities and imaginaries of precision haemato-oncology (Engen 2020). One of Engen's major insights is that irresponsible imaginaries of precision oncology are too gene-centered and do not pay due attention to higher levels of biological organization. CCBIO's mission is in this sense scientific and social at the same time: A key long-term impact of CCBIO, to be assessed in the future, should be the strengthened awareness and understanding of the role of the tumor microenvironment and higher levels of biological organization, among scientists, practitioners and the general public. ••

C. B. N. Engen (2020). Exploring the boundaries of precision haemato-oncology. The case of FLT3 length mutated acute myeloid leukaemia. Dissertation, University of Bergen.

I. W. Nilsen (2019). Kreft, forestillinger og sensasjonsjournalistikk. En analyse av sosio-tekniske forestillinger om kreftforskning i møte med journalistiske nyhetsrammer [Cancer, imaginaries and sensational journalism. An analysis of sociotechnical imaginaries of cancer research meeting journalistic news frames]. URL http://bora.uib.no/handle/1956/20422

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

R. Strand & L. A. Akslen (2017). What is responsible cancer research? Tidsskr Nor Legeforen 2017; 137: 292-4, doi: 10.4045/tidsskr.16.0295.

Research Teams and Programs

For the second term (2018 – 2023), the organization of CCBIO has been modified to reflect the current research activities. We now have four teams and corresponding project areas: basic studies of tumor-microenvironment interactions (Team I), exploration and validation of cancer biomarkers in human tissues (Team II), clinical studies and early trials (Team III), and societal studies including projects on ethics, economics and priorities (Team IV). On top of this, the four programs are supported by resources on bioinformatics and processing of big data, and Rolf Reed is a strategic advisor. Increased collaboration within CCBIO, between the different teams and investigators, has taken place over the years. CCBIO is supported by an International Faculty of 16 top scientists in different fields.

T1

Mechanisms of Tumor-Micro-environment Interactions

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

TEAM 1 → McCormack, Kalland, Gullberg

T1

DONALD GULLBERG

Research focus
The research of the Gullberg group is focused on work related to integrin α11. Integrin α11β1 is a collagen receptor with several features which makes it an interesting molecule in tissue and tumor fibrosis. During almost two decades, the group has accumulated a number of reagents to perform detailed molecular studies of cell-collagen interactions, including several unique transgenic mouse strains all based on the integrin α11 gene. During 2020, a model will be published on the ITGA11-Cre transgenic mouse strain.

Projects
The CCBIO projects deal with deeper knowledge on the role of integrin α11 at the molecular and cellular level in order to better understand its role in the tumor stroma.

1. The major focus has been to develop a new fibroblast specific transgenic Cre driver mouse strain where Cre-recombinase is driven by 3kb of human integrin α11 promoter (ITGA11-Cre strain). Functional characterization of Cre-recombinase in this mouse strain has been determined by crossing with the Rosa 26 Cre reporter strain.

2. A second project relates to the role of integrin α11 in squamous cell carcinoma and is performed in collaboration with Ritva Heljasvaara, University of Oulu. Dr. Heljasvaara is a member of the International Faculty.

3. A third project has just started and will be performed in collaboration with Daniela Costea. This will involve studies of integrin α11 regulation in cancer associated fibroblasts (CAFs) by mechanical stiffness and use of the Hyperion Imaging System to visualize CAF biomarkers in the tumor microenvironment (TME).

Important results
During 2019, the group has published one paper describing the wide distribution of α11 on CAFs in different solid tumors, and a detailed paper describing the importance of integrin α11 cytoplasmic tail for ERK-mediated α11β1 cell signaling. An extensive study, resulting from a productive and stimulating collaboration with Agnés Noël, University of Liege, on the role of α11β1 in the PyMT breast cancer model, was also published in 2019.

Current challenges
In basic integrin research, major questions concern a better and more detailed understanding of molecular mechanisms of integrin function as well as the nature of synergistic integrin activities in biological systems. In the fibrosis field, the challenge is to understand heterogeneity of fibroblasts and CAFs in the tumor stroma as well as the mechanisms that affect the dynamics of different fibroblast states.

Future plans
1.With regard to the ITGA11-Cre mouse strain, the plan is to cross it with a R26R dtTomato mouse strain.
2. The mechanical strain experiments involve mutant CAFs lacking integrin α5, mutant mammary fibroblasts lacking TGFβRII, and syndecan-4-deficient MEFs. The group has observed interesting phenotypes of mutant fibroblasts cultured on surfaces of different stiffness and is in the process of re-transfecting TGFβRII and syndecan-4 to ensure the specificity of the observed effects.

3. The work to further characterize α11 antibodies continue as planned, and epitope mapping of α11 antibodies using mutant integrin α11 variants (domain swapping and deletions) expressed in HEK293 cells are ongoing. ••

GROUP MEMBERS:

Gullberg, Donald, PhD, professor, group leader
Kusche-Gullberg, Marion, PhD, professor
Alam, Jahedul, MSc, PhD candidate
Gyarmathy, Gergő, MSc, PhD candidate
Moses, Musiime, MSc, PhD candidate
Grønning, Mona, chief engineer
Lu, Ning, PhD, senior laboratory engineer

T1

KARL-HENNING KALLAND

Research focus
The Kalland group pursues a drug discovery and development program and dendritic cell-based cryo-immunotherapy (CryoIT) against cancer.

Projects
Drug Discovery and Development: The screening part of this project has utilized both a panel of phytochemicals available in collaboration with Shanghai and a panel of drugs approved for treatment of human and animal diseases according to the repurposing strategy. Luciferase and fluorescent reporter cell lines have been utilized to screen for small molecular compounds that inhibit either β-catenin signaling or STAT3 signaling.

CryoIT: A phase I clinical trial was completed in 2019. The protocol is currently revised in order to conduct next stage clinical trials based upon the important experiences gained regarding safety, treatment effects and biomarkers.

Important results
Drug Discovery and Development: The group's repurposing strategy has identified 2 compounds that inhibit β-catenin signaling in cancer cell lines, and the molecular targets and mechanisms were identified. Further, 3 novel compounds with STAT3-inhibiting activity have been found. Publication is postponed due to the patenting process in collaboration with Shanghai and conducted by VIS (Western Norway Innovation Company).

CryoIT: The Phase I clinical trial was completed this year, and 18 patients with metastatic castration-resistant prostate cancer were included. The primary endpoint of safety and patient tolerance appeared very good. Treatment effects were suggested according to radiology, circulating tumor cell enumeration, large-scale serum auto-antibody profiling and ultradeep T-cell receptor sequencing. Patient follow-up is still ongoing. Highly valuable experience has been obtained regarding both treatment aspects and optimized biomarkers that benefit current planning of next generation CryoIT. Results from interim analyses have been presented at international meetings. The comprehensive results are now analyzed and will be published in 2020.

Current challenges
Great progress of cancer therapy has been achieved in recent years and continues. Still, increases in median overall survival are mostly measured in months rather than in years in clinical trials with new small molecular compounds. Immune checkpoint inhibitors represent the greatest progress and have achieved long-term and maybe curative effects in subgroups of several cancer types. CAR T-cell therapy has revolutionized treatment of B-cell malignancies and is promising for additional cancertypes. In most cases, however, human cancer is still not curable once it has become metastatic. In the group's research projects, they envisage potential improvements both in CryoIT with more potent dendritic cells enhanced with new compounds. Biomarker optimization continues for better prediction and monitoring of therapy.

Future plans
One key focus is the robust production of more potent therapeutic dendritic cells in Bergen for use in next generation CryoIT. In order to achieve this aim, more insight is required into dendritic cell differentiation. The role of β-catenin and STAT3 signaling will be investigated in dendritic cell re-programming in addition to the group's published results on those pathways in tumor initiating cells. In order to better understand immune cell re-programming in the tissue micro-environment, and the effect of combination therapy, the group aims to establish in vivo mimicking of organoid co-cultures ex vivo. Patient tissue and liquid biopsies will be essential both experimentally and for the development of biomarkers. • •

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%)

T1

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 be solved through multidisciplinary development of preclinical surrogates, models and diagnostic tools that more accurately mimic clinical conditions.

Subsequently, the group has led the development of patient derived xenograft models and multimodal imaging for use in the evaluation of novel therapies. Also, lab-on-a-chip scaffolds for greater in vitro understanding of the bone marrow microenvironments have been established.

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 pre-clinically elucidate, evaluate, and potentiate a new era of sonoporation theranostics for PDAC through application of innovative biomarker mining, organoid models and preclinical modeling. Phase II trials are planned, following a very successful phase I trial.

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

Finally, the INOvA project is developing the application of image-guided surgery, whereby fluorescent dyes will target biomarkers on surgically amenable cancers to aid their greater resection. This is particularly relevant to gynecological cancers and sarcomas for which trials are planned.

Important results
The SonoCURE group has demonstrated that sonoporation with gas filled microbubbles impacts the intracellular signaling of cancer cells and identified biomarkers that can be exploited for therapeutic intervention in combination with sonoporation (Haugse et al. Pharmaceutics 2019). In addition, Ragnhild Haugse and Tormod Karlsen Bjånes will defend their thesis in 2020.

The PreLIM group has identified that stabilization of β-catenin upon B-cell receptor signaling promotes NF-kB target genes transcription in mantle cell lymphoma (Baran-Marszak et al. Oncogene, in press). Furthermore, the group has identified novel small-molecule therapeutic targets in mantle cell lymphoma (Gelebart et al. submitted 2019) and initiated collaboration with the Moffitt Cancer Center in the development of several novel cell-based immunotherapeutics. Sahba Shafiee successfully defended her thesis on "Translational Development of Preclinical Models and Therapies in Myelodysplastic Syndromes (MDS)."

INOvA purchased the first preclinical system for Fluorescence Image-Guided Surgery (FIGS) in Scandinavia. This equipment will aid resolution and easier visualization of metastasis, critical in the surgical resection of gynecological cancers. Two manuscripts are under revision (Kleinmanns et al.) following the identification of a novel biomarker overexpressed in approximately 90% of ovarian cancer patients. Two further manuscripts are under review describing the immunogram of ovarian cancer patients by mass cytometry. Katharina Bischof and Katrin Kleinmanns successfully defended their PhD theses in 2019, while Shamundeeswari Anandan and Elvira García de Jalón will defend in 2020.

Current challenges
The major challenge in the group's research area is the relevance and penetrance of the model systems employed for translational research. The advent of immunotherapy and the evolving understanding of the tumor micro-environment has dramatically impacted the way we develop and perform preclinical research.

Future plans
The McCormack group will work to consolidate the different subprojects into one multifaceted research group working at the interface of clinical and basic research. They will endeavor to generate novel immunotherapies based on the biomarkers elucidated through CCBIO and evolve their preclinical modeling platforms to provide state of the art models that impact clinical development of tomorrow's therapeutics.

GROUP MEMBERS:

Senior researchers:
McCormack, Emmet, PhD, professor, group leader
Kotopoulis, Spiros, PhD, senior researcher
Leitch, Calum, MSc, researcher
Langer, Anika, PhD, researcher
Fosse, Vibeke, DVM, veterinarian
Popa, Mihaela Lucia, DVM, veterinarian

Technical staff:
Fandalyuk, Zinayida, MSc, staff engineer, lab manager
Safont, Mireia Mayoral, BSc, staff engineer
Thodesen, Elisa Ulvøen, MSc, staff engineer
Eriksen, May Gjerstad, MSc, staff engineer
de Montlaur, Constance de Villardi, PhD, staff engineer
Benjaminsen, Susanne, MSc, staff engineer
Rozmus, Ezekiel Richard, MSc, staff engineer

Postdoctoral fellows:
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de Garibay, Gorka Ruiz, PhD
Kleinmanns, Katrin, PhD

PhD candidates:
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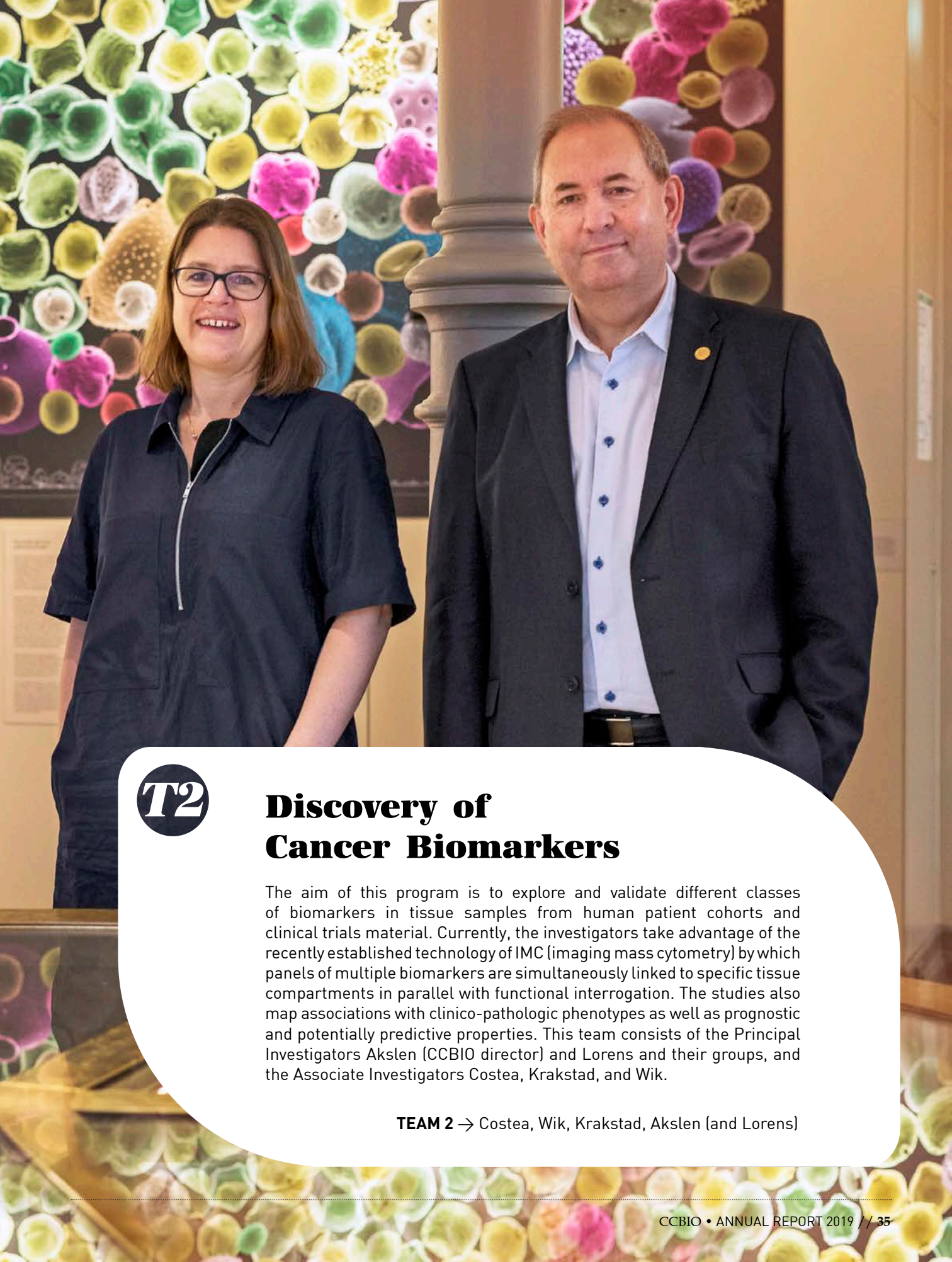
Bergsjø, Louise Emblem, MSc
Bjånes, Tormod Karlsen, MD
Dowling, Tara Helen, MSc
Engen, Caroline Benedicte Nitter, MSc, MD
Haugse, Ragnhild, MSc
Shafiee, Sahba, MSc
Viñegra, Elvira García de Jalón, MSc



T2

Discovery of Cancer Biomarkers

The aim of this program is to explore and validate different classes of biomarkers in tissue samples from human patient cohorts and clinical trials material. Currently, the investigators take advantage of the recently established technology of IMC (imaging mass cytometry) by which panels of multiple biomarkers are simultaneously linked to specific tissue compartments in parallel with functional interrogation. The studies also 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 Costea, Krakstad, and Wik.

TEAM 2 → Costea, Wik, Krakstad, Akslen (and Lorens)

T2

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. The group has concentrated on the mapping of protein patterns by using tissue compartment specific proteomics analyses (Mass Spectrometry) and imaging mass cytometry (CYTOF)

Projects
1. Proteomics portraits of breast cancer subtypes stratified by tumor cell and microenvironment compartments

2. Markers of neuro-angiogenic phenotypes in breast cancer and associations with immune responses and molecular phenotypes

3. Role of nestin and stathmin as markers of BRCA1-related, basal-like and aggressive breast cancer

Important results
Proteomic profiling of laser captured 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 reprogramming, and differential activation of tumor-based stimulation of the microenvironment, such as angiogenesis.

Transcriptomics data, supplemented by protein expression information and cell line studies, indicate that angiogenic, immunogenic, and neurogenic responses appear to be coordinated and different between breast cancer subtypes. These phenotypes also differ according to basic clinico-pathologic characteristics and disease progression and might provide novel biomarkers and targets for more precise patient management.

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, and also associated with stemness and angiogenic profiles. After CRISPR-based knockdown of nestin in aggressive breast cancer cells, marked changes in proteomic profiles have been observed, and animal experiments are ongoing to characterize tumor growth and metastatic spread in vivo. Further, data have shown that stathmin expression is a marker associated with nestin, and also related to angiogenic and immunogenic responses in aggressive breast cancer.

Current challenges
A major challenge in the field of tissue profiling is to account fully for the complexity and heterogeneity within malignant tumors. Future in situ studies need to improve information on spatial resolution of molecular data, using different endpoints such as targeted 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.

Future plans
In the Akslen group, projects will further explore the phenotypic diversity in breast cancer, with special focus on tumor-microenvironment characteristics and functional interactions. Cancer tissues 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 researcher
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

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Finne, Kenneth, PhD
Kleftogiannis, Dimitrios, PhD
Schuster, Cornelia, MD, PhD
Vethe, Heidrun, PhD

PhD candidates:
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Børretzen, Astrid, MD
Chen, Ying, MD
Ingebriktsen, Lise M., MSc
Kjølle, Silje, MSc
Pilskog, Martin, MD
Smeland, Hilde Ytre-Hauge, MD
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Pre-PhD projects:
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Svanøe, Amalie, stud.med.
Tegnander, Amalie, stud.med.

Technicians:
Ardawatia, Vandana, PhD, senior engineer
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Kalvenes, May Britt, PhD, senior engineer
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T2

JAMES B. LORENS

Research focus

The Lorens group discovered that the AXL receptor tyrosine kinase is an essential regulator of tumor EMT, of acquired drug resistance, and of the anti-tumor immune response. Although seldom mutated, AXL expression in tumors is a universal poor prognostic factor for patient outcomes. AXL is also a critical negative regulator of innate immune cell responses and is expressed by suppressive myeloid and tolerogenic dendritic cells in the tumors. The group's recent results are translated phase II clinical trials.

Most cancer patients will not experience lasting benefits from current therapies. The Lorens group discovered that AXL is a key driver of acquired drug resistance. By uncovering the molecular mechanism of AXL regulation of the tumor micro-environment, in concert with combination clinical trials with AXL targeting agents, a new paradigm to improve cancer treatment has emerged.

Projects and important results

AXL in tumor-immune crosstalk

Tumor suppressive myeloid cells are a primary obstacle to immunotherapy. The Lorens group's recent results show that AXL inhibition improves immune checkpoint inhibitor efficacy by blocking both tumor EMT and immune suppressive cell mechanisms. High dimensional mass cytometry demonstrated that AXL-expressing tumor suppressive myeloid cells were targeted by bemcentinib treatment. The group's findings indicate that AXL signaling integrates cancer cell plasticity with immune suppressive myeloid and regulatory dendritic cell mobilization and that tumor immunity can be enhanced by combined ICB and AXL targeting.

AXL in acquired cancer therapy resistance

The group's recent studies demonstrate that AXL signaling allows tumor cells to resist cytotoxic T-lymphocyte (CTL)-mediated cell killing by abrogating immune synapse formation, a prerequisite for the success of immunotherapeutic approaches. AXL signaling abrogates NK/CTL-mediated killing by decreasing ICAM1 surface expression that destabilizes the immune synapse. AXL inhibition stabilizes NK/CTL conjugation. These results suggest that AXL targeting will optimize T-cell-mediated anti-tumor immune responses.

As acquired cancer therapy resistance evolves under selection pressure of immune surveillance, it is expected that mechanisms which promote drug resistance through cell survival and immune evasion will be favored. The group found that EGFRi resistance in lung cancer was mediated by upregulation of AXL. Mass cytometry revealed cell signaling heterogeneity is incompatible with a simple bypass signaling mechanism. AXL inhibition abrogated cytoprotective autophagic flux and induced immunogenic cell death in drug resistant NSCLC. AXL and autophagy gene signatures were correlated in a large cohort of human NSCLC. The group's results show that AXL signaling supports a drug resistant persister cell phenotype through a novel autophagy dependent mechanism and reveals a unique immunogenic effect of AXL inhibition on drug resistant NSCLC cells.

Current challenges

Identifying biomarkers and therapeutic vulnerabilities in the tumor micro-environment that address resistance to current targeted and immunotherapies is a major focus in the field.

Future plans

The Lorens group will focus on determining how AXL receptor signaling regulates tumor intrinsic resistance to immunotherapy. They hypothesize that GAS6–AXL complexes have unique signal transduction attributes that support pro-survival and cytotoxic T-cell resistant cell states. They address this through systems-level signal transduction analysis, and high dimensional single-cell mapping of phenotypic-spatial features of the tumor microenvironment in cancer patient biopsy samples from ongoing phase II clinical trials. ••

GROUP MEMBERS:

Senior researchers:
Lorens, James, MS, PhD, professor, group leader
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Chen, Ying Yi, researcher
Engelsen, Agnete, MS, PhD, researcher

Postdoctoral fellows:
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Madeleine, Noëlly, PhD, postdoc
Lotsberg, Maria Lie, PhD, postdoc

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Kang, Jing, MD

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Grøndal, Sturla Magnus

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Berge, Sissel Vik, chief engineer
Stigen, Endre, staff engineer
Lu, Ning, senior engineer, 50%
Siraji, Muntequa Ishtiaq, staff engineer, 50%

T2

DANIELA COSTEA

Research focus
Understanding the role of epithelial-mesenchymal interactions in carcinoma progression and identification of micro-environment-related prognostic bio-markers.

Projects
1. Mechanisms of tumor-stroma interactions including metabolic coupling.

2. Understanding the role of tumor stroma in drug resistance.

3. Stroma as a source of prognostic biomarkers.

Important results
The Costea group has shown, for the first time, that carcinoma cells are able to induce a unidirectional mitochondrial exchange from normal neighboring fibroblasts (Zhang et al, Cell Mol Life Sci, 2019), in addition to increased L-lactate production and oxidative stress via induced hypoxia, mitophagy and mitochondrial permeability transition pore opening, leading to their metabolic re-programming. These metabolic alterations can be further exploited for metabolically addressed targeted therapy towards the stromal tumor compartment. Of particular interest is that the group showed that the metabolic reprogramming of the fibroblasts occurs before their activation and conversion into a carcinoma-associated (myo)fibroblast phenotype and was not accompanied by cellular senescence.

Another novel finding was that the metabolically reprogrammed neighboring fibroblasts were able to rescue carcinoma cells from the metformin-induced apoptosis through inhibiting the activity of AMPK and PARP, maintaining mitochondrial membrane potential and increasing the oxidative stress (Zhang et al, Cell Cycle, 2019). The results indicate that metformin effects on cancer cells are modulated by the microenvironment, and this must be taken into consideration in the context of developing a new combination of drugs for cancer treatment including metformin.

Together with the research group of Professor Line Bjørge, the Costea group has established novel experimental models of vulvar carcinogenesis and revealed that also in this cancer type, the stromal fibroblasts play a key role for tumor progression (Dongre et al, Exp Cell Res, 2019).

Current challenges
The group's results point towards complex interactions between carcinoma cells, carcinoma associated fibroblasts, immune cells and endothelial cells. The challenge is how to decipher these interactions and what experimental models should be used and established that are sufficiently elaborated to mirror the complex in vivo tumor, but feasible enough for individual analysis and modulation of its different components in order to reveal their respective contribution to drug resistance and tumor progression.

Future plans
The group's core activities will continue towards understanding the tumor-stroma interactions, and how they can be used for personalized therapy. The focus will be on deeper characterization of the fibroblast heterogeneity and how this differentially influences tumor progression and drug resistance in HPV positive and negative cancers. ••

GROUP MEMBERS:

Senior researchers:
Costea, Daniela Elena, DDS, PhD, professor, group leader
Johannessen, Anne Christine, MD, DDS, PhD, professor
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Manrikyan Gayane, DDS
Papian, Andrew, MD
Zhuoyuan, Zhang, DDS

Technicians:
Fromreide, Siren, MSc
Kalvenes, May Britt, PhD

T2

CAMILLA KRAKSTAD

Research focus
The Bergen Gynecologic Cancer Research group focuses on molecular profiling of gynecological malignancies, with a special focus on identifying new biomarkers for endometrial and cervical cancers. Among the group's interests are also the establishment of improved preclinical model systems for endometrial cancer, to generate tools that enable functional studies and evaluation of biomarker expression in relation to treatment.

Projects and important results
Blood-based biomarkers are attractive due to ease of sampling and standardized measurement technology, reducing obstacles for clinical implementation. The group has identified blood metabolites and steroids associated with poor prognosis in endometrial cancer. Elevated steroid levels are linked to increased estrogen signaling and fat distribution. The focus on steroids in blood samples adds to the group's continuous focus on hormone receptors in endometrial cancer. The MOMATEC2 study, a phase 4 implementation trial for validation of ER/PR status as a stratifier for lymphadenectomy in endometrial cancer, is ongoing and inclusion of patients from international centers is increasing. During 2019, the Krakstad group performed the first interim analysis with focus on biomarker cut-offs (from 2015-2017).

During the past few years, the group has done extensive work to improve mouse models for endometrial cancer, and this work is continuously in focus. They have, in collaboration with the McCormack group, developed a new NIRF-based imaging method that enables detection of patient derived tissues in mice models (Fonnes et al, under review). This method is currently routinely used alongside imaging methods like FDG-PET and MRI to monitor treatment responses in mice models.

The Krakstad group continues its focus on preoperative patient imaging parameters derived from PET-CT and/or MRI as important biomarkers. In close collaboration with Professor Ingfrid Haldorsen at the Mohn Medical Imaging and Visualization Center, they integrate imaging data, clinical information and genetic data in large scale radiogenomic analyses.

Current challenges
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 highly important. In recent years, much attention has been on identification of molecular subgroups of endometrial cancer. Following the TCGA report on endometrial cancer, efforts have been made to design a clinically relevant molecular classifier, and biomarkers like MSI status, P53 and POLE mutations are becoming implemented at many pathology departments. However, one key challenge is still to link these subgroups to relevant treatment and thereby improve patient treatment and outcome.

Future plans
The group will continue to develop their molecularly defined models for endometrial cancer and will also shift focus more to the use of these models for drug testing, functional experiments and exploration of subtype specific genetic alterations. They will expand their biomarker focus and exploit the potential for immunohistochemical multiplexing available through the Hyperion equipment. The MOMATEC2 trial will be completed in collaboration with the currently contributing national and international centers. ••

GROUP MEMBERS:

Senior researchers:
Krakstad, Camilla, professor, MS, PhD, group leader
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Haldorsen, Ingfrid, MD, PhD, adjunct professor

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Jacob, Havjin, MSc, PhD
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Madissoo, Kadri, MSc
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Medical Student Research Program students:
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Myrvold, Madeleine

T2

ELISABETH WIK

Research focus
Associate Professor Elisabeth Wik (consultant pathologist) heads the group Breast Cancer of the Young - Bergen (BCY-B), established in 2019. Their research focuses on breast cancer of the young, a group that experience more aggressive tumors and poorer survival compared to what is expected based on traditional clinico-pathologic prognostic measures. Unraveling the underlying age-related biology is clinically highly relevant to improve understanding and clinical handling of this patient group.

Projects
1. Estrogen receptor-related biology in breast cancer of the young

2. Landscape of immuno-phenotypes and potential age-related differences

3. Risk of recurrence score (ROR) in breast cancer of the young

4. Germline and somatic DNA repair mutations in breast cancer of the young

5. Targets for therapy in primary tumors and metastatic lesions in breast cancer of the young

Important results
The project "Breast Cancer of the Young; Age-Related Biology" is in its early phases. One major achievement has been the establishment of a large clinical cohort of breast cancer of the young, including tissue material, histopathologic annotations, and long and complete follow-up data. The first paper from this cohort is in pre-submission phase (A. Svanoe et al.).

Current challenges
In general, cancer biomarker research is under pressure by a requirement to demonstrate bio-functional relevance of the markers under study. When hunting the direct link(s) between biological functionality and the biomarker under study, it is important to keep in mind the biological complexity and the clonal evolution that takes place, as important hallmarks of cancer. Validation studies have to be conducted to bring discoveries closer to clinical applications.

Future plans
The group plans to explore the tumor microenvironment with age-related biological differences in focus, in collaboration with CCBIO's international faculty. Established methods such as imaging mass cytometry (Hyperion) and the NanoString technology will be increasingly used. Also, building an international network with researchers on breast cancer of the young is one of the goals for the group in the years to come. ••

GROUP MEMBERS:

Wik, Elisabeth, MD, PhD, associate professor, group leader

PhD candidates:
Sæle, Anna Kristine Myrmel, MD
Ingebriktsen, Lise Martine, MS

Medical Student Research Program students:
Svanøe, Amalie
Hugaas, Ulrikke
Tegnander, Amalie Fagerli

T3

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.

TEAM 3 → Straume, Bjørge, Gjertsen

T3

BJØRN TORE GJERTSEN

Research focus
The Gjertsen group focuses on intracellular signal transduction in conventional and targeted therapy and questions how signal transduction in cancer cells and stromal or immune cells may act as biomarkers. These represent biomarkers for response or non-response in patients before and early after start of therapy. Such an aim calls for special infrastructure of patient selection and sample logistics. Clinical trials with strict sample procedures and logistics have proven to be necessary to test these hypotheses.

Projects
Subprojects include single cell immune and signaling profiling of patients with chronic myeloid leukemia, acute myeloid leukemia and selected solid cancers, using samples of peripheral blood from patients in clinical trials. The group's data indicate that chronic myeloid leukemia responds homogenously to kinase inhibitors directed to their driver oncogene BCR-ABL1. Acute myeloid leukemia is a heterogenous disease where the spread in responde to a single kinase inhibitor is wide, however, the response to intensive chemotherapy is more homogenous. Lymphocytes in both leukemia and solid cancers may contain information of response to immune therapy, and this should be determined more in detail.

Important results
Optimalization of protein-based biomarker panels for mass cytometry has been reported (Gullaksen SE et al. Cytometry A 2019). This technology was used in acute myeloid leukemia for multi-parametric single cell evaluation. The group defined distinct ex vivo drug responses in healthy hematological cells that are retained in corresponding malignant cell types (Majunder MM et al. Haematologica 2019). Based on ex vivo drug responses, the group tested the therapeutic effect of a novel combination with interferon alpha and valproic acid (Forthun RB et al. J Cancer Res Clin Oncol 2019). Interestingly, in vivo experiments in rat and mouse showed no benefit of the combination valproic acid and interferon alpha, in contrast to similar tumor cells treated in culture. This is an example of how in vivo experiments demonstrate a lack of effect, or even detrimental effect on overall survival, similar to what has been seen repeatedly in clinical trials. These results ended the group's ambitions for clinical development of this combination of interferon alpha and valproic acid. However, biomarkers based on phosphorylated proteins appeared optimal for following therapy.

Current challenges
The costliest cancer therapy is the therapy that does not work. Based on examples from small subsets of leukemic diseases like chronic myeloid leukemia and acute promyelocytic leukemia, biomarkers may secure targeted therapy for responders with high accuracy. Contemporary biomarkers are dominated by genomic tests, and to some degree, single proteins detected in histopathological tumor sections. The Gjertsen group addresses functional biomarkers and biomarker panels in tumor and contextual cell types, seeking a more precise response prediction.

Future plans
The group's focus in the coming years will be to examine if tumor cells, support cells or immune cells comprise the most useful information for response determination in AML patients treated with the AXL inhibitor bemcentinib. Preliminary results based on clinical trials in chronic and acute myeloid leukemia, as well as immune therapy in various solid tumors, are now evaluated and validating mass cytometry experiments will be performed on clinical samples collected from specific clinical trials. ••

GROUP MEMBERS:

Researchers:
Gjertsen, Bjørn Tore, MD, PhD, professor, group leader
Andresen, Vibeke, MSc, PhD, senior researcher
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Gullaksen, Stein-Erik, MSc, PhD
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Motzfeldt, Inga Kristine Flaaten, Msc
Nguyen, Rebecca
Sabir, Misbah, MSc
Wangen, Rebecca, MSc

Administrative support:
Hjelle, Sigrun Margrethe, MSc, PhD

T3

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
1. 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 nonresectable (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.

2. 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.

3. 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.

4. 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 tissue biopsies.

5. Research project: Importance of physical trauma on time to recurrence after primary treatment of breast cancer, by analyzing patient series and blood samples from patients undergoing different types of breast surgery. 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.

6. Research project: The role of epithelial-to-mesenchymal transition (EMT) and cancer stem cell traits in breast cancer metastasis, by analyzing the role of the EMT associated AXL receptor in initiation and progression of breast cancer.

7. Research project: Targeting cancer stem cells with AXL receptor inhibitors to improve the treatment of cancer, by using different preclinical models to study efficacy of the AXL inhibitor BGB324 in cancer. In particular, the combinations of BGB324 with immune check point inhibitors are encouraging.

Important results
Some selected results from the projects above:

1: Overall, 54 patients have received treatment in the trial as of Jan 2020, and five regional centers have recruited patients. In June 2019, an interim analysis showed that the treatment was safe, and inclusion continues.

3: In melanoma patients treated with bevacizumab, circulating tumor DNA (ctDNA) detected by digital droplet PCR was a useful biomarker for both monitoring and predicting response to bevacizumab.

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

5: The group has quantified surgical complications occurring after breast reconstructions in breast cancer patients and results show a significant change in recurrence dynamics in patients who experience complications.

Current challenges
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. We 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 disease. We need to increase our understanding on why micro-metastatic foci of cancer cells escape from dormancy and cause overt metastatic disease.

Future plans
The group will continue collecting data and patient materials (blood/tissues) in clinical trials. A new phase 2 clinical trial in renal cell carcinoma combining cryoimmune therapy with immune checkpoint inhibitors will be initiated. ••

GROUP MEMBERS:

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

LINE BJØRGE

Research focus and projects
Insight into the molecular background of high-grade serous ovarian carcinoma (HGSOC) is growing, and molecular (BRCA, HRR deficiencies) and phenotypic profiling (platinum sensitivity, degree of debulking) is beginning to be integrated into clinical trials and practice. The introduction of PARP inhibitors to frontline treatment is believed to translate into an overall survival benefit. Further improvements will require rethinking, and a roadmap for research priorities has been outlined.

Over the last decade, the group has established a multidisciplinary research portfolio focusing on HGSOC, called Rethinking Ovarian Cancer (RETHINK). Through a focus on biomarkers, preclinical models, and early-phase clinical studies, the aim is to translate data from comprehensive profiling into strategies that improve personalized patient care. The portfolio is divided into four programs: Experimental preclinical models, Tumor microenvironment, Image-guided surgery and Clinical translation (trials).

Together with the McCormack group, the Bjørge group has established the INOvA team (Innovative Novel Ovarian cancer treatment Approaches). All the results presented here are generated by the INOvA group. The gynecologic cancer unit at Haukeland University Hospital, Bergen, Norway, is an integrated part of this group, and a European Training Center in Gynecological Oncology. All in vitro and in vivo preclinical work is performed at the group's laboratories and the clinical trials take place at the hospital's trial units.

Important results
The group has established tools for deep-tissue profiling, a comprehensive range of xenograft models, and early-phase studies with modern design. These discoveries represent the foundation of ongoing and future projects. Their two-investigator initiated early-phase clinical study is still ongoing, and during 2019, two of the group's students have defended their PhD thesis.

Current challenges
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 wellbeing and quality of life, is critical.

Future plans
Inherent tumor biological characteristics of HGSOC influence the effect of different therapies (surgery, chemotherapy, targeted therapeutics), and the ability to select more individualized treatment establishment and validation of preclinical platforms for deep-tissue profiling, as well as drug screening is necessary. This can be achieved through the application of the comprehensive profiling program Bjørge's group is establishing. Given the importance of surgery, a tumor targeted fluorescence-image guided surgery methodology will be further developed. Objectives include a generation of an HGSOC organoid platform, definition of the TME of HGSOC by means of the cancer immunogram, development of Fluorescence Image Guided Surgery (FIGS), preclinical evaluation of the targeted therapeutics, and identification of biomarkers for treatment selection. ••

GROUP MEMBERS:

Bjørge, Line, MD, PhD, MBA, professor, group leader
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Thomsen, Liv Cecilie Vestrheim, MD, PhD, postdoc
Fosse, Vibeke, DVM, veterinarian

T4

Health Ethics, Prioritization and Economics

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

TEAM 4 → Cairns, Norheim, Strand

T4

ROGER STRAND

Research focus
Strand's group performs research on the ethical, legal and societal aspects (ELSA) of CCBIO's 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 smallscale 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 AFINO, and Horizon 2020 SuperMoRRI and TRANSFORM). They are furthermore performing 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 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, asking whether that perspective can be reverse engineered into the search and design of biomarkers.

Current challenges
There is the challenge of practical relevance. Research in the field of Science and Technology Studies has produced thousands of pages of excellent empirical studies and theoretical analyses of the challenges and opportunities of modern medicine and modern medical research. During the latter 15 years, we have also been challenged 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.

Future plans
The main short-term plan is to publish a synthesis of the insights from the group's collaborations within team IV (with CCBIO ethicists Norheim and Tranvåg, and economists Cairns and Kang) and from collaborations with the other CCBIO teams (Wik, Akslen, Dillekås, Engen, Gissum and others). Specifically, the Strand group is working on a book project that follows up on their 2017 volume "Cancer Biomarkers: Ethics, Economics and Society".

CCBIO has entered its second 5-year period. Before 2023, the group's challenge is to create a level of ELSA awareness in CCBIO as such, and to have made 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, and with international collaborations. CCBIO can in many ways be seen as "best practice" for RRI. It is important for the Strand group to translate their work in CCBIO into contributions to the wider field of RRI and governance of science.••

GROUP MEMBERS:

Strand, Roger, dr.scient., professor, group leader
Bremer, Anne (née Blanchard), PhD, researcher
Stenmarck, Mille Sofie, cand. med., guest researcher
Nilsen, Irmelin W, M. Phil., guest researcher

T4

OLE FRITHJOF NORHEIM

The Global Health Priorities Research Group that Ole Frithjof Norheim leads, has in 2019 grown and developed into a center - the Bergen Centre for Ethics and Priority Setting (BCEPS). With funding from the Bill & Melinda Gates Foundation, Trond Mohn Foundation, Norad and the University of Bergen, BCEPS aims to study the ethics and economics of priority setting in health services. Its main area of focus is decision support for universal health coverage in Ethiopia, Malawi and Zanzibar.

Although with a strong global health focus, BCEPS is also committed to work on priority setting challenges in Norway. The collaboration with CCBIO on cancer biomarkers, precision medicine and fair priority setting is central to this aim.

Research focus
The aim of CCBIO is to discover, validate and translate cancer biomarkers, a key component of precision medicine. Norheim's group is interested in how cancer biomarkers can inform and hopefully improve health care priority setting. How is our ethical thinking about treating people as equals challenged when biomarkers and other individual characteristics stratify patients into smaller and smaller sub-groups, with only some being offered new and potentially life-saving treatments?

Projects
The group 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. 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, the role of patient age in clinical decision making is examined and provides a base for important future work.

Current challenges
The increasing amount of new and expensive cancer drugs entering the market offer opportunities, but also challenges. With often marginal effect and unreasonable and confidential pricing, these drugs will impose a heavy burden on our publicly financed health care system. Also, it is not clear how biomarker tests, next generation sequencing and other diagnostics should be assessed in the reimbursement system.

Future plans
The group will continue to 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 CCBIO's 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

T4

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). Also, a new PhD project has been undertaken by Jiyeon Kang entitled: Improving economic evaluation and decision-making for oncology drugs using real-world data.

Important results
Mikyung Kelly Seo and Ana Beatriz Luis completed a paper which explored the evidence for whether the use of cancer biomarkers to guide treatment had improved 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.

Mikyung Seo submitted her PhD thesis entitled Economic Evaluations of Cancer Biomarkers for Targeted Therapies at the end of 2019. Part of this research was with CCBIO colleagues assessing the cost-effectiveness of HSP27 as a biomarker in the treatment of metastatic melanoma.

John Cairns published a study of cancer drug reimbursement decisions in six European countries.

Current challenges
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.

Future plans
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.

The PhD candidate Kang will continue her review of the one hundred and sixty evaluations of oncology drugs undertaken by NICE in the past ten years. The study documents the increasing use of real world evidence. She will be exploring a number of hypotheses regarding the use of real world data by manufacturers in their evidence submissions and the acceptability of such evidence to decision makers. ••

GROUP MEMBERS:

Cairns, John, MA, MPhil, professor, associate investigator, group leader
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
Kang, Jiyeon PharmD, MSc, 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 and development of methods to exploit the novel Hyperion technology to the study of tumor-microenvironment interactions in solid cancers.

Projects
Jonassen is leading a project funded by ERAPerMed, including as partners Professor Gjertsen from CCBIO in addition to groups from Germany, the Netherlands and Canada. A postdoc has been recruited to work on this project in Jonassen's group. The project includes 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. At the end of 2019, a new postdoc position within the Jonassen group was announced – to work on development and use of methods to exploit the novel Hyperion imaging technology to the study of tumor-microenvironment interactions.

Important results
Relevant to Jonassen's work in CCBIO, he published (in bioRxiv) in 2019 a study of gene expression in Parkinson's disease where it was shown that changes in cell composition confound expression signatures so far found to be associated with the disease. This was found by using a deconvolution approach utilizing previously known cell type signatures – an approach complementary to that earlier developed by the Jonassen group in context of CCBIO. This provides an improved basis for the work also within CCBIO in the coming period.

Current challenges
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.

Future plans
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, the group plans new efforts utilizing the Hyperion imaging platform, potentially together with single cell omics approaches to improve the understanding of tumor-microenvironment interactions. ••

GROUP MEMBERS:

Jonassen, Inge, MS, PhD, professor, group leader, associate investigator
Kleftogiannis, Dimitrios, postdoc
Wimalarasan, Akilina, master student

Strategic Advice

ROLF REED

Professor Rolf K. Reed stepped down as PI during 2018 and entered into a role as strategic adviser to CCBIO for the second term. His commitment towards CCBIO is the same as when he was PI in parallel with being head of the Department of Biomedicine. Reed still has students and research activities in CCBIO and is affiliated to the Lorens group.

The stepping down as PI came as a natural result of a wish to devote more time to tasks at a strategic level in general, also outside of CCBIO. The strategic advisory role will benefit from a long experience of leadership positions and strategic committees at the University of Bergen, as well as having been dean, deputy dean and head of department for many years. Reed's long experience with committees and planning groups in research councils, international evaluation and advisory boards will be brought into the longtime strategic planning in CCBIO, both for the remaining duration of the Centre as well as for the continuation when the ten year core funding from The Research Council of Norway expires in 2023.

Among the commissions of trust held by Reed during 2019, were chair of the Committee for Science Advice for Policy at the Norwegian Academy of Science and Letters and chair of the board at the Center for Advanced Studies at the Norwegian Academy of Science and Letters.

Research activities

The research activities are currently focused on a collaboration on PDX-models with Professor Linda Stuhr. Another ongoing project is the turnover of potential biomarker proteins, such as sAxl, in the intact organism to understand how it is turned over by transport through the circulatory-interstitial-lymphatic system. The project is performed together with Professors Lorens and Tenstad at the Department of Biomedicine.

The results from a long-time project was concluded and published last year while on sabbatical. The project studied the potential use of MRI-based gadolinium tracers for use in experimental cancers in mice in order to determine capillary transport parameters in these experimental cancers (Curry FE, et al.; Acta Physiol 2019). ••

International Faculty

The CCBIO International Faculty was established to support the Centre through active collaborations and strategic advice. In addition to the 13 members below, three additional members (Marta Bertolaso, Rome, Italy; Jonathan Irish, Nashville, USA; Ursula Klingmüller, Heidelberg, Germany) were recruited during 2019, and they are now in the final stages of formal appointment.

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 framework 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, Amant 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.

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

Jean-Christophe Bourdon

Dr. Jean-Christophe Bourdon 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 the Breast Cancer Campaign in 2012.

Dr. Bourdon's research group is internationally recognized to have pioneered and developed the p53 isoform research field, which has reformed and broadened the p53 field beyond cancer to ageing and age-related degenerative diseases. Research interests are both in basic 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 aims to establish the p53 isoforms as predictive biomarkers and to identify new therapeutic compounds targeting the p53 isoform pathways. Dr. Bourdon has developed a large panel of p53 isoform-specific antibodies enabling to investigate the p53 protein isoforms expression and activities in clinical samples (FFPE-IHC, flow-cytometry). Dr. Bourdon made the antibodies available to the scientific community and pharmaceutical companies.

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 anti-cancer and anti-metastatic inhibitor of AXL receptor kinase inhibitor developed at CCBIO (BGB324). Bourdon would like to further extend 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.

Rolf A. Brekken

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

Professor Rolf A. 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. Professor Brekken's laboratory is focused on understanding how the tumor microenvironment effects therapeutic efficacy. Two therapeutic antibodies Brekken helped develop, have entered clinical testing in cancer patients. In collaboration with Dr. Jim Lorens, the Brekken Lab validated the efficacy of AXL inhibition with bemcentinib in preclinical models of pancreatic cancer, laying the foundation for an ongoing clinical trial, testing bemcentinib and chemotherapy in pancreatic cancer patients.

Professor Brekken's laboratory is focused on three general areas: 1. Tumor cell plasticity; 2. Therapeutic immune reactivation; 3. ECM signaling.

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

Klaus Pantel

Professor Pantel did his MD at the University of Cologne in 1986 on Mathematical Modeling, his Dr. Med. at the University of Cologne in 1987 and his Dr. Med. Habil. at the Ludwig-Maximillians-Universität on Cancer Immunology in 1995. Klaus Pantel is currently the founding director of the Institute of Tumor Biology at UKE (established in 2002), and he has conducted ground-breaking work at the forefront of translational and clinical research on "early tumor cell dissemination/minimal residual disease" and liquid biopsy in patients, both in bone marrow and in the circulation. The American Society of Clinical Oncology and College of American Pathologists Joint Review Committee recently considered him as a founder of the liquid biopsy field of research. This contribution was also acknowledged by the Open Plenary Lecture at the 2018 Annual AACR Meeting in Chicago. Liquid biopsy has the potential to initiate paradigm changes in clinical practice leading to improved cancer therapies. Dr. Pantel has published 531 papers on cancer metastasis and liquid biopsy, including original reports in leading clinical translational journals (e.g., NEJM, Lancet, Lancet Oncology, JCO, JNCI, Cancer Discovery, Science TM and CCR) and several expert reviews in Nature journals, and his work has been credited with an h-index of 95. He received several awards for his pioneering work, including the 2010 German Cancer Award (most prestigious award for cancer researchers in Germany) for Translational Research, and the 2010 AACR Outstanding Investigator Award for Breast Cancer Research. He shows a very high dedication to multinational collaborations as demonstrated by his common publication and grants with excellent researchers in Europe, USA, Australia and Japan. He has been the principal investigator of translational European networks focusing on liquid biopsy, e.g. the Cancer ID EU/IMI consortium (2015-2019), the ERA-NET TRANSCAN "Prolipsy" (2018-2021) and two European Research Council (ERC) Advanced Investigator Grants with two additional ERC POC grants (2019-2024 and 2011-2016). Besides the establishment of international research networks and bi-annual symposia on liquid biopsy and MRD, he has organized a unique infrastructure with large patient cohorts at the Comprehensive Cancer Center Hamburg (UCCH) of the UKE in Hamburg, which supports the translational, patient-oriented research of his team. Over the past 20 years, he has established a metastasis/liquid biopsy network that includes > 40 UKE departments.

As adjunct professor at the University of Bergen, 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 cryo-immunotherapy 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. ••

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. In October 2019 he moved to an exciting new role as Chief Medical Officer of BerGenBio in Bergen, offering an opportunity to work with the BerGenBio team to drive forward AXL targeted clinical development. 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.

In his new role at BerGenBio, Gabra intends to foster collaborations with the CCBIO, particularly around translational and clinical research for AXL targeted therapy.

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 the Queen's University of Belfast and is John Black Associate Professor of Prostate Cancer at the University of Oxford. In addition, he is a visiting scientist at the 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 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 several 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.

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 Faculty of Biochemistry and Molecular Medicine (FBMM), University of Oulu, and is currently the co-director of the group. From the beginning of 2020 she acts as the director of the ECM-Hypoxia Research Unit at the FBMM. The unit consists of five strong research groups, which formed part of the Finnish Centre of Excellence in Cell-ECM Research of Academy of Finland in 2012-2017, and are now actively participating in efforts to promote the University's research profile in the ECM, hypoxia 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, especially collagens, in skin, breast, lung and hematologic malignancies. The most promising of the ongoing projects pursue the roles on non-fibrillar collagens in breast cancers, and the crosstalk between the cancer cells and osteoblasts in acute myeloid leukemia. In collaboration with Professor Donald Gullberg, Dr. Heljasvaara is

using mouse models to investigate the role of the fibroblast-specific integrin α11 in solid cancers, especially in skin squamous cell carcinoma. The key findings show that α11 is upregulated in skin tumor stroma and has a supportive role in skin tumorigenesis with effects on carcinoma-associated fibroblast differentiation, ECM organization and tumor stiffness.

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 Dean of Postdoctoral Training at the Beckman Research Institute at City of Hope National Cancer Center, California.

Professor LaBarge's principle interests are to understand the role of the 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 Jim Lorens which has taken shape in three main areas. First, the teams have been using high-dimensional single cell CyTOF-based analyses to quantify 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 and luminal progenitors, which are thought to be breast cancer cells of origin. 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 micro-environment-driven signaling in single cells, which they are now using to understand how the perception of the microenvironment changes with age and transformation. Finally, in work that includes also the labs of Lars A. Akslen, Rolf Brekken, Nils Halberg, 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.

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 the 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 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 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.

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 are investigating the role of immune cells in DCIS and their impact on risk for progression from DCIS to invasive breast cancer.

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, which has been licensed to Vigeo Therapeutics and is currently in clinical trials in the United States.

Dr. Watnick has a longstanding collaboration with Lars A. 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. The Watnick lab also 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.

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 the tumor micro-environment 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), and he also acted as coordinator for the Swedish Research Council-supported STARGET center-of-excellence 2006-16.

Since the adjunct professor appointment at UiB in 2015, Östman has obtained two rounds of 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 Donald 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, Solstrand (Os) close to Bergen in 2019, and will be continued with a 2020 meeting in the southern part of Sweden. Östman also contributed with one chapter to the recent collection of reviews on tumor microenvironment edited by Akslen and Watnick.

Research School for Cancer Studies

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. Under the leadership of Elisabeth Wik, the CCBIO RSCS has flourished with several new activities. RSCS courses are available for all researchers, PhD students and master-level students, also outside of CCBIO.

The CCBIO RSCS is well established as a scientifically stimulating and inclusive meeting place for students and researchers within various areas of cancer- and ELSA-related research, with a common focus on translational studies of cancer biomarkers. PhD candidates and postdocs get the opportunity to meet and discuss their research projects across the established teams and disciplines. CCBIO has successfully integrated the RSCS into its strategic activities, like the CCBIO Annual Symposium, CCBIO Junior Scientist Symposia and CCBIO Research 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 2019, CCBIO held the courses that run continuously (CCBIO901 and CCBIO902), as well as CCBIO903 and BMED904. Also, CCBIO907, the new course on cancer-related vascular biology, completed its third course week in 2019. A new course on Clinical Trials in Cancer Research with integrated Good Clinical Practice certification was also introduced. The very successful two-day Scientific Writing Seminar by Christine Møller and Randy Watnick was repeated in 2019 and was also this time oversubscribed. Read more about these activities in seperate chapters.

For 2020, the CCBIO Research School plans to run CCBIO906 (February); CCBIO904 (April), the Scientific Writing Seminar (May), CCBIO907 (September), and CCBIO905 (October).

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. These events are described in detail in separate chapters of this annual report.

CCBIO903 – Cancer Research: Ethical, Economic and Social Aspects

The two week 5 ECTS course CCBIO903 has been held four times since 2015 and is a unique opportunity for PhD candidates – not only those who are part of CCBIO, but also national and international students – to question the assumptions underlying their PhD work, reflect on and discuss the robustness of their research, and anchor it in a broader social, cultural, political, economic and ethical context. The core of the course is structured around the volume edited by Anne Bremer and Roger Strand: *Cancer Biomarkers: Ethics, Economics and Society* (2017). Some of the key questions addressed during the course are:

- What are the promises, limitations and consequences of the "imaginary" of precision cancer medicine?
- What is a "good enough" cancer biomarker in that context? What are the opportunities and limits of biomarkers, and when do we think we know enough?
- How do we take medical decisions when faced with risks, uncertainties and even ignorance?
- In a highly medicalized culture, what does a "good life" look like for (future) cancer patients?
- What is 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?

To facilitate and encourage such reflections, the course has several unique features:

1. The course is highly interactive, and the lectures invite the participants to take part in extended reflexive discussions with the teaching team and among themselves. At the end of the course, all candidates are asked to present their work in relation to broader social and/or economic aspects.

2. The teaching team is highly interdisciplinary. In addition to having a teaching team from different disciplines (philosophy of science, science and technology studies, and health economics), several guest lecturers are invited to share their perspectives. For the 2019/20 edition of the course, we for instance had Caroline Engen, Hanna Dillekås and Elisabeth Wik, from clinical and medical science; Eirik Tranvåg, from the ethics of prioritization of care group; and Jiyeon Kang from health economics.

3. The course rounds up with a special seminar, open to all, with an expert panel who discusses in depth a specific issue related to cancer. On the 9th of January 2020, the special seminar was on "*Cancer in the news*", with presentations from Mille Stenmark (MD) and Irmelin Nilsen (master in media studies), and extensive discussions with panelists Tine Dommerud (journalist at Aftenposten) and Knut Helland (from the Department of Information Science and Media Studies, UIB).

In 2019, the first week of CCBIO903 was held in December and the second week was planned for January 2020. The participants came from a great variety of backgrounds (ranging from medical and clinical science, to health economics and nursing, plus more for the open lectures) and geographical locations, such as Bergen, Oslo (Oslo University Hospital, Institute for Cancer Research), Finland (University of Eastern Finland), London (London School of Hygiene and Tropical Medicine) and Boston (Boston Children's Hospital). CCBIO903 is co-organized and taught by three members of the ELSA and Economics groups in CCBIO: Roger Strand, Anne Bremer and John Cairns.

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.

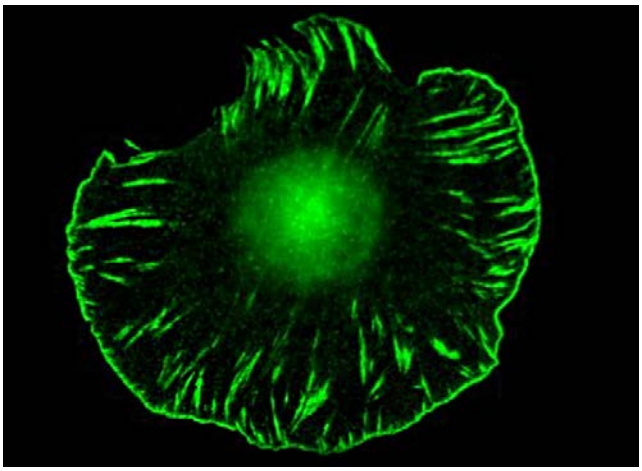
Upon completing this course, the candidate should have the skills to:

- 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.

To pass, the candidates need to participate in 90% of the lectures, 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 and hospitals. Oddbjørn Straume has the academic responsibility and Reidun Kopperud is the course coordinator. The next course will be held April 21-23, 2020.

BMED904 – Matrix Biology
BMED904 is a 3 ECTS well-established course from the Bergen Biomedical Research School (BBRS) that has been included into CCBIO's course portfolio as a joint effort with the 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. In 2019, three of the lecture highlights included John Couchman (Copenhagen), Cathy Merry (Manchester, UK) and Joanna Philips (UCSF, San Francisco). 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 are demonstrated. The course has been evaluated as excellent by the participating students, and as well organized, with inspiring and interesting lectures giving a good overview of the ECM and its importance in heath and disease.



The course was last held June 3-7, 2019, where fourteen students signed up for the course. Attending students were from Bergen, other cities in Norway and from Finland.

The next course will be in June 2021, 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. In 2020, a new theme, the role of cancer associated fibroblasts in cancer and ECM, will be covered. 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. The next course will be in the fall term of 2020.

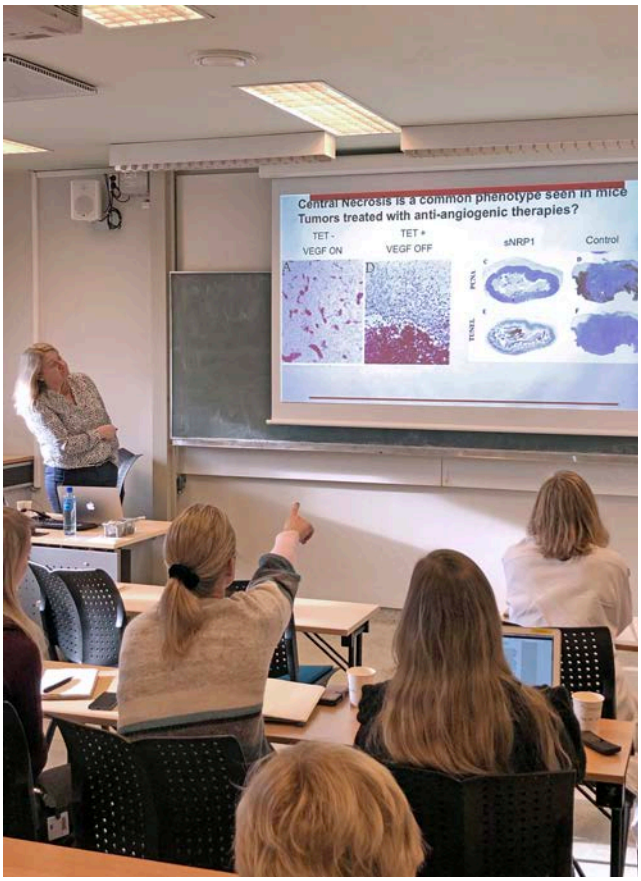
CCBIO906 – Cancer Genomics
CCBIO906 is a 3 ECTS course providing a broad understanding of aspects in cancer genome biology and their investigation by next generation sequencing (NGS) technologies, and applications as biomarkers for diagnostics and treatment. Methods for analyzing DNA variation and structure 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 participants should have knowledge regarding what kinds of mutations may predispose for, contribute to, or appear during cancer development, how these variants can be detected by NGS methods and be analyzed bioinformatically, how to employ these methods to stratify patients both diagnostically and therapeutically, the different implications of the same aberrations depending on tissue type, and ethical and legal regulations regarding genetic analyses of patient samples. They should have the skills to formulate problems, plan and carry out NGS analyses on samples from cancer patients, be able to assess the expediency and application of different NGS methods in cancer diagnostics and research, to know the contact points for NGS analysis and data storage and analysis in the Bergen area, and to be able to communicate relevant literature and methods concerning cancer genomics.

To pass the course, the candidate must be present at least 90% of the course, participate actively in the group, and pass an online exam.

CCBIO906 was first held November 1-3, 2017, and the next will be in February 2020, with 41 students enlisted. Ola Myklebost has the academic responsibility, and Rebecca Nguyen is the course coordinator.

CCBIO907 – Cancer-Related Vascular Biology
CCBIO907 is a new three-week course (6 ECTS) covering topics such as basics of vascular biology, vascular biology related therapeutic approaches, biomarkers in vascular biology – from discovery to clinical application, lymph-angiogenesis and vascular biology in non-cancerous diseases. Students attending this course benefit from the experienced lecturers



from Harvard Medical School who have been in the frontline of vascular biology research for decades.

This course provides a broad theoretical and practical understanding of basic aspects of vascular biology, cancer-related vascular biology, and other processes and diseases where vascular biology is relevant. The course presents knowledge about relationships between vascular biology, cancer progression, and diagnostic and treatment options directed towards the vasculature. Applied methods for studying vascular biology and biomarkers reflecting cancer-related vascular biology are also taught. The course aims to stimulate scientific thinking and professional discussions.

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

Upon completing this course, the candidate should have:

- Knowledge about basic vascular biology, principles and challenges related to personalized medicine, cancer-related vascular biology and how this knowledge is applied within cancer treatment today as well as the status of frontline research of vascular biology,

ways of exploiting knowledge of vascular biology in search for new treatment strategies, and cancer-related biomarkers in cancer diagnostics and treatment.

• The skills to formulate hypotheses to plan and conduct studies on cancer-related vascular biology, consider utility and limitations in use of cancer-related biomarkers and be able to communicate relevant literature and methods concerning cancer-related vascular biology, with critical reflection.

• The ability to evaluate how knowledge about vascular biology can assist in understanding tumor biological processes and mechanisms, and use it as a guide to improved diagnosis, targeted treatment and follow-up of cancer patients.

In order to pass, the candidates need to participate in 80% of the lectures, prepare for and participate actively in the group assignments, and prepare an oral presentation together with the group.

CCBIO907 was held for the first time 2018/2019. Elisabeth Wik and Lars A. Akslen have the academic responsibility. The next course will run in the fall term of 2020.

CCBIO-VBP Lab Visit Program

CCBIO and the Vascular Biology Program (VBP) at Boston Children's Hospital and Harvard Medical School established a Lab Visit Program in 2018, as part of the CCBIO-INTPART activities. Here, CCBIO students at master and PhD levels have been offered a summer internship at VBP labs. In 2018 and 2019, three students attended this program both years, each with 8-12 weeks of lab visits. Both PhD candidates and students from the Medical Student Research Program participated. In 2018, Silje Kjølle, Amalie Svanøe and Martha Rolland visited the labs of Randy Watnick, Marsha A. Moses and Michael Rogers. In 2019, Amalie Fagerli Tegnander, Ridhima Das and Hanna Dillekås joined the labs of Randy Watnick, Diane Bielenberg and Michael Rogers at VBP. The students learned a range of different lab techniques, improved their presentation skills and critical paper reading, and were included in discussions on planning experiments. The CCBIO students joining the VBP labs unanimously reported that they were warmly welcomed by the PIs and other colleagues at the host labs. By participating in lab meetings, observing other fellows' presentations and the feedback they got, the students were stimulated to be curious and ask questions, and they observed how critical discussions brought the scientific work forward.

Being part of a top-notch scientific environment stimulates to pursue ideas and ambitions and excel your own standards - like Professor Bruce Zetter previously have encouraged scientists to do (2018; at the CCBIO seminar entitled "What is Scientific Excellence").

Joining the Lab Visit Program has been educational, challenging and inspiring, and all CCBIO students attending have reported great educational and scientific benefits from their summer in Boston. The networking with students and faculty at VBP have been rewarding for the students, and likely of great value for the students' future research careers.

Scientific Writing Seminar

CCBIO launched a two-day seminar on scientific writing in December 2017. Since the seminar was fully booked shortly after its announcement, it was repeated in May 2019 and was once more oversubscribed with around 100 enlisted for 80 available spaces. Both years, master students, PhD students, postdocs, medical students, researchers and technical staff attended the seminar, and gave stellar reviews.

The seminar covered topics such as organizing ideas, improving the manuscript, clear writing, scientific storytelling, titles and abstracts, cover letter, common mistakes and making a manuscript memorable. Lecturers were Christine Møller, an experienced lecturer in medical and scientific writing with many years of experience as assistant editor of APMIS (Acta Pathologica Microbiologica et Immunologica Scandinavica), and Randy Watnick, a CCBIO international faculty from Harvard Medical School. The 2020 course will in addition add Medical Faculty Media Advisor Marion Solheim with a lecture on science presentation, showing how to make a presentation stick in a good way. She will also talk about the use of language, information overload and layout, as well as body language and tone of voice.

The scientific writing seminar is now an integrated part of the CCBIO RSCS's activities and we expect attendance at the upcoming course in 2020 to be as good as for the previous years. Elisabeth Wik is coordinator of the Scientific Writing Seminar.

Clinical Trials in Cancer Research
This is a new course in the portfolio of the CCBIO RSCS, first organized October 3-4, 2019. The course is designed to prepare the participants to conduct clinical trials on humans. Clinical trials are studies performed in humans, aimed at evaluating one or more medical, surgical or behavioral intervention(s), and such trials is the primary method to determine whether a new treatment is safe and effective, and whether companion biomarkers can be applied to stratify patients for novel therapy. Usually, a clinical cancer trial compares the most effective known treatment for a specific type or stage of cancer with a new approach, although other designs are used increasingly frequently. Today there are clinical trials for almost every type of cancer, and the numbers are increasing. While many trials focus on late stage disease, there are also trials for cancer prevention and early diagnosis, and prevention of recurrence and survival.

The course consists of 6 different modules. The first day covers general principles, operations, formalities and regulations. The second day focuses on success factors and clinical trials in the future. The Clinical Trials in the Future session was open for a wider audience as a CCBIO Special Seminar. Lecturers at the 2019 course came from UiB as well as other national and international institutions. 68 participants attended the 2019 course, ranging from researchers, postdocs and students to technical staff and study nurses.

The course is not applicable for ECTS, but the modules included are based on the ICH GCP, and the participants receive a certificate in Good Clinical Practice on completion of the course.

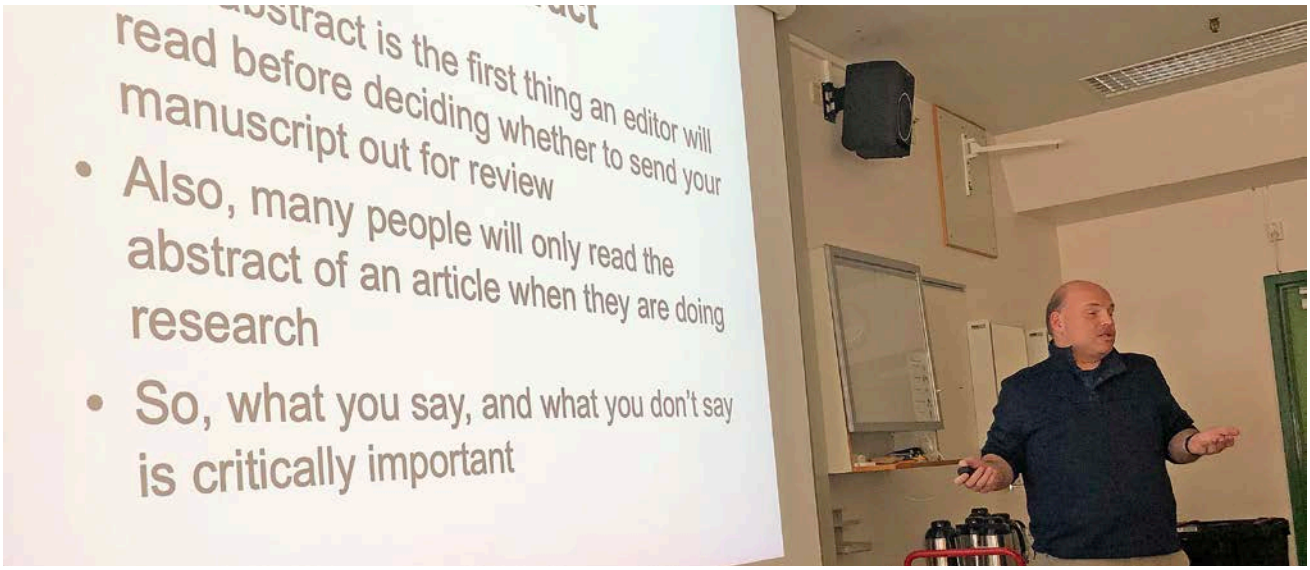
The course is led by Line Bjørge, who has the academic responsibility together with one of CCBIO's International Faculty, Hani Gabra, from the Imperial College of London. Reidun Kopperud is the course coordinator.

International Collaboration and Further Development of Courses
CCBIO has strong emphasis upon internationalization, as most of the CCBIO groups have a research portfolio that is inherently international. From the start in 2013, CCBIO has aimed to move beyond the usual internationalization measures. As a part of this focus, we have recruited an international network of adjunct researchers that take actively part in our projects as well as with lectures and tutoring of younger researchers, in the CCBIO courses and larger meetings.

The CCBIO International Faculty frequently take part as lecturers in the CCBIO RSCS courses. External international and national faculty are also invited as lecturers. Hence, CCBIO's own, as well as other students and researchers, get the possibility to meet and interact with influential experts in the cancer research field.

The CCBIO RSCS aims to continue and further develop the excellent courses (CCBIO901-907) and other established activities. Additionally, in 2020 we aim to develop a course focused on "Research-related innovation" to be launched during the 2021 spring semester.

As part of CCBIO's internationalization efforts, a project under the the RCN and DIKU funded program for International Partnerships for Excellent Education and Research (INTPART), has been set up in collaboration between CCBIO and faculty from the Vascular Biology Program (VBP),



Boston Children's Hospital, Harvard Medical School, and Harvard Kennedy School. The INTPART activities are used to foster stronger integration between excellent teaching and research environments in collaboration with international partners. In addition to including master level students into CCBIO RSCS activities and integrating INTPART with other existing activities, new INTPART activities like the CCBIO907 Cancer-Related Vascular Biology course, the Scientific Writing Seminar, the Boston lab visit program and several seminars and meetings have been established.

The INTPART projects and collaboration is directed through a partnership between CCBIO (directed by Lars A. Akslen) and the VBP in Boston (directed by Marsha A. Moses). Elisabeth Wik is the INTPART coordinator in Bergen, with Randy Watnick, Assistant Professor at VBP and Harvard Medical School and Adjunct Researcher in CCBIO's international network, as the coordinator in Boston. In addition, Assistant Professor Michael Rogers is the VBP coordinator for CCBIO907, and also co-coordinated the CCBIO-VBP Research Meeting at Iceland together with Elisabeth Wik (main coordinator).

All the activities under the CCBIO-INTPART program have been very well received among students at our faculty, and we would like to highlight the following:

- Students attending the Scientific Writing Seminar have proposed the seminar as mandatory for all students at the PhD level. CCBIO aims to run this seminar yearly, at least until CCBIO's CoE core funding ends in 2023.
- The CCBIO907 course Cancer-Related Vascular Biology was very well received by the students attending the first course (2018-2019). Faculty from the VBP inspired and challenged the Bergen students. CCBIO907 will be held next in September 2020.
- The lab visit program between CCBIO and the VBP at Boston Children's Hospital and Harvard Medical School was established in 2018, for students at master and PhD levels. Several students from the Medical Student Research Program have attended this activity also in 2019. The students attending have reported great educational and scientific benefit from their Boston stay. Further stays are planned for 2020.
- A 4-day CCBIO-VBP Research Meeting was held at Iceland in 2019. Faculty and students from both CCBIO and VBP actively participated in the meeting. Further collaboration, educational as well as scientific, was discussed and established during the meeting. (Read more about this in a separate section.)

Researcher Training

The centrally organized part of CCBIO's researcher training is the CCBIO Research School for Cancer Studies (RSCS), led by Associate Professor Elisabeth Wik. The RSCS is a scientifically stimulating and inclusive meeting place for junior scientists within cancer research and has a common focus on translational studies of cancer biomarkers. It also serves as a bridge to CCBIO's ELSA efforts. In both courses and other research school activities, PhD candidates and postdocs meet and deliberate upon their research projects across the established groups. Several of the courses and other activities are well suited for master and PhD students also from areas outside of cancer research.

CCBIO stimulates postdocs to increasing independence and they are encouraged to provide guidance to younger researchers within the different CCBIO research groups.

Throughout 2019, CCBIO had a total of 55 PhD students, of which 67% were female. Roughly half were of Norwegian origin and among the remainder, Africa and Asia were particularly well represented with about a third.

KATHARINA BISCHOF
"Rethinking Gynecological High-Grade Serous Carcinoma. Portraying the p53 isoform landscape and development of a new preclinical tool for optical imaging in xenograft models." Supervisors: Professor Line Bjørge, Professor Emmet McCormack, Professor Bjørn Tore Gjertsen and Researcher Stian Knappskog.

MARIA LIE LOTSBERG
"The role of AXL and the microenvironment in cancer cell plasticity and therapy responses. A study in non-small cell lung cancer models." Supervisors: Professor James B. Lorens, Professor Lars A. Akslen and Researcher Agnete S.T. Engelsen.

SAHBA SHAFIEE
"Translational Development of Preclinical Models and Therapies in Myelodysplastic Syndromes (MDS)." Supervisors: Professor Emmet McCormack, Associate Professor Astrid Olsnes Kittang and Professor Bjørn Tore Gjertsen.

SIGMUND YTRE-HAUGE
"Advanced imaging biomarkers in endometrial cancer." Supervisors: Professor Ingfrid S. Haldorsen, Professor Jone Trovik and Professor Helga B. Salvesen (†).

MARIA RYSSDAL KRABY (NTNU)
"Tumor Vasculature in Subtypes of Breast Cancer." Supervisors: Professor Anna Bofin, Associate Professor Signe Opdahl, Professor Lars A. Akslen and Researcher Hege Russnes.

KJERSTI TEFRE DAVIDSEN
"The Receptor Tyrosine Kinase AXL in Tumour Phenotyptic Plasticity and Acquired Resistance to Cancer Targeted- and Immunotherapy." Supervisors: Professor James B. Lorens and Professor Oddbjørn Straume.

KATRIN KLEINMANNS
"Rethinking High-Grade Serous Ovarian Carcinoma: Development of New Preclinical Animal Models for Evaluation of Image-guided Surgery and Immunotherapy." Supervisors: Professor Emmet McCormack and Professor Line Bjørge.

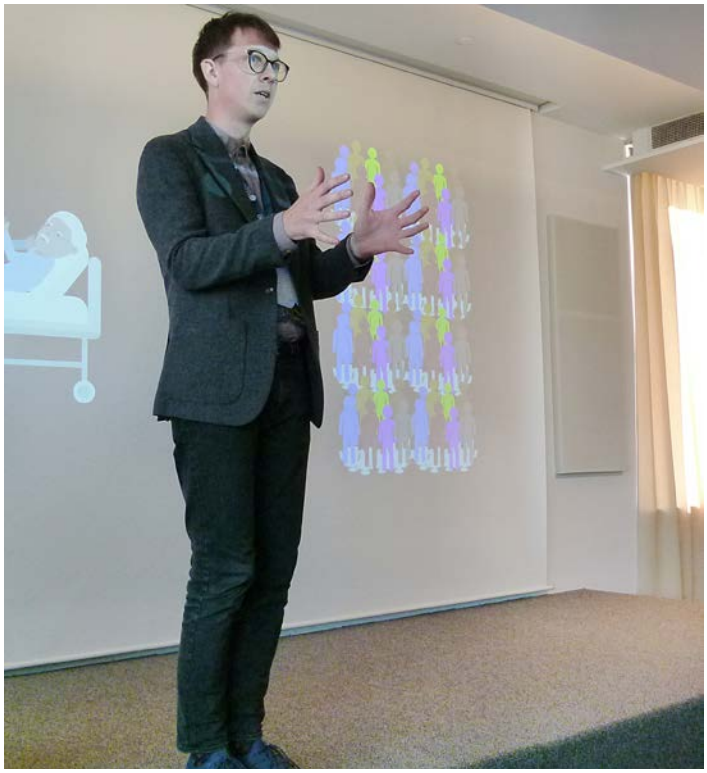
SAMEER BHARGAVA
(Cancer Registry of Norway & UIO)
"Mammographic screening among immigrant women in Norway; disparities in attendance and selected screening outcomes." Supervisors: Professor Solveig Hofvind, Associate Professor Kåre Moen and Professor Lars A. Akslen.

CCBIO
RESEARCH SCHOOL
FOR CANCER STUDIES

Junior Scientist Symposium

The CCBIO Junior Scientist Symposium (JUSS), which also constitute the PhD course CCBIO901, aims to let junior scientists present their research in an environment of peers, and provide the opportunity for feedback across disciplines. JUSS is arranged four times a year. The setting is friendly and acts as a practicing arena for participants to ask relevant questions and generate academic discussions. Students, postdoctoral fellows, staff and visitors are all welcome to the Junior Scientist Symposia.

Throughout the seminar series, researchers in their early career are encouraged to practice relevant skills for a future academic career, including oral presentations in front of an audience, as well as scientific writing. The participants are also introduced to critical evaluation of ethical aspects in daily work and reflection about communicating their research to the public and media. Students signed up for the CCBIO901 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 or her own method(s) at one of these meetings. During 2019, four



symposia were arranged with 25-35 participants each. The programs included presentations from PhD candidates, postdoctoral fellows and other researchers as well as inspirational lectures by senior researchers such as Professor Inge Jonassen, Professor Charalampos (Haris) Tzoulis and Harald Barsnes from the University of Bergen and Carina Strell from Karolinska Institutet, Stockholm. Providing insight into how successful research careers can develop, motivates young scientists to find their own path.

Throughout the year, the high-quality presentations by PhD students and postdoctoral fellows, the enthusiasm of presenters and the audience, and the fruitful discussions during the breaks, makes the Junior Scientist Symposia an encouraging and outstanding experience for participants and organizers alike.

In 2019, the Junior Scientist Symposium was organized and chaired by the postdoctoral fellows Kenneth Finne, Liv Cecilie Vestrheim Thomsen (spring), and Cornelia Schuster (fall).• •

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
February 14, 2019
Conference room BBB

Symposium Chairs:
Liv Cecilie Vestrheim Thomsen and Kenneth Finne

10:00-10:05 Organizers: Welcome and information about CCBIO901

10:05-10:25 Stacey D'Mello Peters: "Studying GAS6-AXL RTK signaling by mass cytometry"

10:25-10:45 Harsh Dongre: "microRNA deregulation in Squamous Cell Carcinomas of Oral and Vulva: role of stromal microRNAs in tumour progression"

10:45-11:05 Monica Hellesøy: "A high throughput library screen of potential drug combination candidates for the AXL inhibitor bemcentinib (BGB324) in acute myeloid leukemia"

11:05-11:20 Coffee/tea break

11:20-11:40 Silje Kjølle: "Hypoxia response and stromal hypoxia in breast cancer"

11:40-12:00 Eirik J. Tranvåg: "Precision drugs in the Norwegian reimbursement system"

12:00-12:30 Lunch break

12:30-13:15 Inge Jonassen, keynote: Inspirational lecture

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
April 4, 2019
Conference room BBB

Symposium Chairs:
Liv Cecilie Vestrheim Thomsen and Kenneth Finne

10:00-10:05 Organizers: Welcome and information about CCBIO901

10:05-10:50 Charalampos "Haris" Tzoulis, keynote: Inspirational lecture

10:50-11:05 Coffee/tea break

11:05-11:25 Pouda Panahandeh: "Targeting sphingolipid pathway in breast cancer"

11:25-11:45 Sigrid Nakken: "Transcriptomic characterization of renal cell carcinoma patients with progressive disease despite low initial risk of progression"

11:45-12:05 Heidrun Vethe: "Regeneration of beta-cells for diabetes cell therapy"

12:05-12:40 Lunch break

12:40-13:00 Kjersti Hestetun: "Is CDX2 an important biomarker in non-metastatic colorectal cancer?"

13:00-13:20 Kristine Aasebø: "Is CDX2 an important biomarker in metastatic colorectal cancer?"

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
September 19, 2019
Auditorium B301, Haukeland University Hospital

Symposium Chairs:
Kenneth Finne and Cornelia Schuster

10:00-10:05 Organizers: Welcome and information on CCBIO901

10:05-10:50 Harald Barsnes, keynote: "How to welcome the new era of public research data"

10:50-11:05 Coffee/tea break

11:05-11:25 Henriette Ertsås: "Science Outreach - How and Why?"

11:25-11:45 Synnøve Nymark Aasen: "Effective treatment of metastatic melanoma by combining MAPK and PI3K signaling pathway inhibitors"

11:45-12:05 David Erik Forsse: "Interim analysis in MoMaTEC2; adjusting cutoff for hormonal receptors"

12:05-12:45 Lunch break

12:45-13:35 Kjersti Davidsen: "Immunotherapy for cancer stem cells. A perfect match?"

13:35-13:55 Maria Lotsberg: "Molecular mechanisms of AXL mediated drug resistance in NSCLC"

13:55-14:00 Organizers: Wrap-up and concluding remarks

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
November 7, 2019
Conference room BBB

Symposium Chairs:
Kenneth Finne and Cornelia Schuster

10:00-10:05 Organizers: Welcome

10:05-10:50 Carina Strell, Karolinska Institutet, Stockholm, keynote: "Investigating the impact of stromal components on breast DCIS progression and treatment response"

10:50-11:05 Coffee/tea break

11:05-11:25 Hanna Dillekås: "Genetic regulation of melanoma latency and angiogenic response"

11:25-11:45 Amalie Tegnander: "Summer internship in the Vascular Biology Program, Boston Children's Hospital - and my AGR2 and AGR3 Project"

11:45-12:05 Ridhima Das: "Isolation and characterization of cells derived from Human Epithelial Rests of Malassez"

12:05-12:45 Lunch break

12:45-13:05 Ole P Nordbø: "miRNA and mRNA sequencing of tumor and metastasis from low risk clear cell renal cell carcinoma patient"

13:05-13:25 Noëlly Madeleine: "Vitamin K influences therapeutic resistance in melanoma"

13:25-13:30 Organizers: Wrap-up and concluding remarks

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 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 pages and circulated by means of round-mails, posters and various newsletters, reaching researchers well beyond CCBIO. This ensures that the CCBIO Seminars are well visited by participants on all levels from a wide range of UiB and hospital departments.
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CCBIO Seminars in 2019

31.01.19 // Cord Brakebusch, Biotech Research and Innovation Center (BRIC), University of Copenhagen, Denmark. Title: Epigenetic control of skin inflammation.

21.02.19 // Diane Bielenberg, Assistant Professor, Vascular Biology Program, Boston Children's Hospital, Department of Surgery, Harvard Medical School. Title: Targeting Neuropilin Pathways to Inhibit Metastasis.

28.03.19 // Gaoxiang Ge, Shanghai institute of Biochemistry and Cell Biology, Chinese Academy of Sciences, Shanghai, China. Title: Extracellular Matrix Remodeling in Tissue Homeostasis and Diseases.

25.04.19 // Øystein Rekdal, PhD, from Lytix Biopharma AS and The Arctic University of Norway, Tromsø. Title: From Bench to Bedside with a first in class oncolytic peptide.

23.05.19 // Valerie Weaver, Center for Bioengineering and Tissue Regeneration, Department of Surgery, University of California San Francisco (UCSF), San Francisco, CA, USA. Title: Forcing tumor risk, transformation and aggression.

06.06.19 // Joanna Phillips, UCSF Department of Neurological Surgery, Helen Diller Cancer Center, University of California San Francisco, CA, USA. Title: GBM heterogeneity and extracellular regulation of oncogenic signaling.

05.09.19 // Sushma-Nagaraja Grellscheid, Associate Professor at the Department of Biological Sciences (BIO), University of Bergen, on the topic of RNA splicing. Title: Understanding alternative splicing regulation in health and disease.

26.09.19 // Karl Kadler, Director at the Wellcome Trust Centre for Cell-Matrix Research, Manchester, UK. Title: Circadian control of the secretory pathway is a central mechanism in tissue homeostasis.

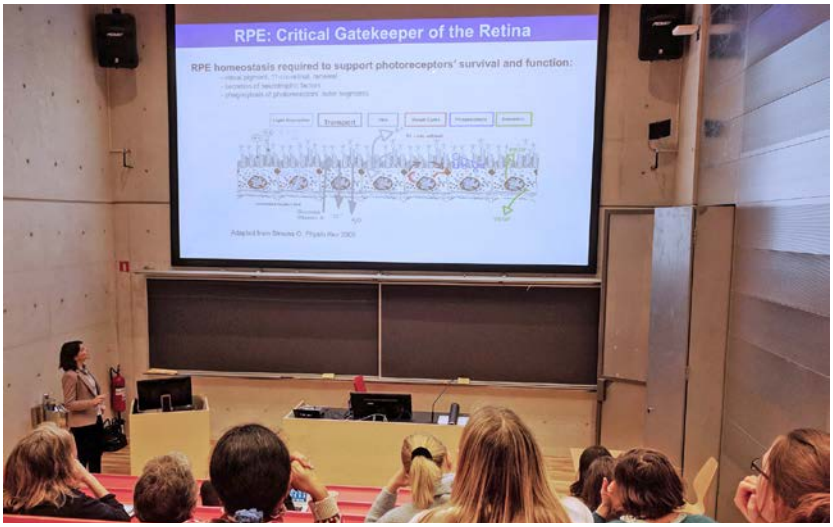
31.10.19 // Daniela Elena Costea, Associated Investigator at CCBIO and Professor in tumor pathology, Department of Clinical Medicine, Faculty of Medicine, University of Bergen. Title: Conditional expression of HPV16 E6/E7 onco-proteins and PIK3CA is sufficient to initiate HPV-associated carcinogenesis.

28.11.19 // Curzio Ruegg, Department of Medicine, Faculty of Science, University of Fribourg, Switzerland. Title: Chemotherapy-induced immunological dormancy in breast cancer.

12.12.19 // Anders Goksøyr, Department of Biological Sciences (BIO), University of Bergen. Title: From feminized fish to obese mice – On endocrine and metabolic disruption in wildlife (and the lab).

CCBIO Special Seminars and Mini-Symposia

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 and Mini-Symposia. Special Seminars are extra-curricular talks more or less of the same format as ordinary CCBIO Seminars whereas the CCBIO Mini-Symposia are longer meetings of two to three hours with multiple speakers elucidating different aspects of a given topic. Both formats 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. 2019 was an active year with a wide range of topics and our special seminars are typically very well visited.



21.02.19 // Shining Light on the Metabolic Control of Retinal Diseases. CCBIO Special Seminar organized as part of the CCBIO/Harvard INTPART partnership, with speaker **Magali Saint-Geniez** from Harvard Medical School and Schepens Eye Research Institute of Massachusetts.

Functional maturation depends on the induction of a specific metabolic program able to support the energetic requirements of specialized tissues. Conversely, metabolic dysfunction can drive cellular reprogramming and transdifferentiation. While establishment and maintenance of retinal pigment epithelial cells (RPE) phenotype is crucial to retinal homeostasis, the molecular mechanisms governing RPE metabolic and functional maturation are unknown. Dr. Saint-Geniez' lecture described recent work from her group's laboratory establishing PGC-1α as a core regulator of RPE mitochondrial function and highlighting the critical role of oxidative metabolism and mitochondrial health in controlling RPE phenotype and retinal functions.

01.04.19 // New trends in clinical sequencing in oncology. CCBIO Special Seminar exploring new trends in clinical sequencing and circulating tumor DNA. Key speaker was an expert in human genome sequencing, **Professor Andre Rosenthal**, CEO and founder of NOEMA Sequencing LLC, Berkeley, CA, USA. Professor Rosenthal explained how clinical sequencing in oncology is very demanding, both on the technical side as well as in the analysis and interpretation of the results. This is mainly due to the low amount of tumor DNA present in tumor tissue and liquid biopsy samples. In many routine oncology samples, less than 5-10ng of tumor DNA is present. In addition, there is always a mixture of normal DNA and tumor DNA. In tumor tissue samples, the tumor fraction must be enriched by macro- or microdissection of pathology slides to reach more than 20 or 30%. This requires additional pathology skills not always available in central sequencing facilities. In liquid biopsy samples, the tumor DNA fraction is often less than 1% or 0.1%. The tumor DNA cannot be enriched prior to sequencing. Special barcoded sequencing assays are required, including highly optimized library prep and target enrichment methods. A coverage of 5,000- to 20,000-fold for the entire gene panel is also required. In addition, tumor tissue

DNA extracted from formalin-fixed paraffin-embedded (FFPE) samples is often highly degraded, which adds to the complexity. Professor Rosenthal described how the newly developed NGS assays provided by Roche can be used in the best possible way for clinical and research applications in oncology, depending on the amount and quality of the sample type available. Local geneticist **Randi Hovland** contributed with her clinical trials experiences. The seminar was a CCBIO and Helse Vest joint meeting.

18.06.19 // Marine bioactive compounds as a source for new anticancer drugs. CCBIO Special Seminar by speaker **Jeanette Hammer Andersen**, professor in marine bioprospecting and head of the natural products platform Marbio at the University of Tromsø (UiT).

Marbio is a high capacity analysis platform for screening and identifying unique bioactive molecules isolated from marine material. Marbio is looking for e.g. enzymes and enzyme inhibitors and substances that can kill cancer cells, are immunosuppressive or immunostimulatory or inhibit the growth of bacteria and viruses.

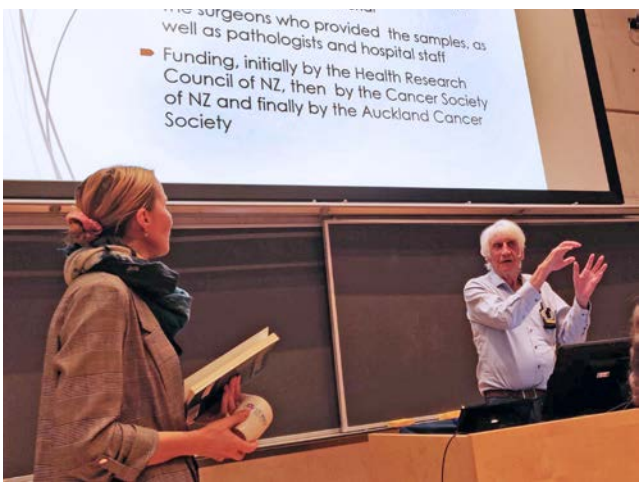
Professor Andersen explained how the success of natural products in drug discovery is unparalleled, more than 60% of the new chemical entities introduced into the clinic originated from, or were inspired by, natural products. Even so, many pharmaceutical companies turned away from natural products as a source of lead compounds, due to the perception that natural products are both difficult to access and to work with. As the marine environment and its organisms have become more accessible over the last decades, it is expected that the ocean will be the next great source of novel chemistry. The rate of new marine natural products discovered is increasing every year.

Marbio at UiT explore Arctic and sub-Arctic marine organisms, searching for compounds with activities against cancer, bacteria and diabetes as well as compounds with immunomodulatory and antioxidative effects. Their screening campaign has been based on a classic bioassay-guided fractionation approach. Professor Andersen explained how they are screening a unique collection of cold-water invertebrates and marine microorganisms and have identified several novel bioactive structures in the collection. The presentation gave an overview of the workflow in Marbio and some of their results from the anticancer screening program.

15.08.19 // Innovation in Cancer Therapy. CCBIO and Helse Bergen invited to a Mini-Symposium on innovation, responding to the public and governmental request for personalized medicine in cancer care. A team of investigators from CCBIO has taken the initiative to form a Centre for Research Based Innovation, aiming to form a unique ecosystem of large and small biotech companies where research is closely linked to the clinical practice. Built around clinical trials in cancer, this flagship center will assemble expertise from preclinical research, bioinformatics, and exploratory biomarkers to accelerate personalized medicine. The mini-symposium presented small and larger bio-techs, big pharma and the research institute sector with some of their strategies, hopefully leading to inspiration for innovation career development among our young investigators and students.

Speakers were:

- Alden Cancer Therapy II - ACT II, by **Karl-Henning Kalland**, CEO, Professor, MD & PhD. Title: Cancer cryoimmunotherapy (CryoIT).
- BerGenBio by **Gro Gausdal**, PhD, Director of Research and Bergen Site Leader. Title: Targeting AXL to treat cancer.
- **DC Prime** by **Richard de Heer**, Director of Business Development and Finance. Title: Relapse vaccines in cancer treatment.
- KinN Therapeutics by **Emmet McCormack**, CEO, PhD, Professor. Title: Preclinical models for validation of targeted therapy and immunotherapy.
- Pfizer by **Cathrine S. Notland**, Medical Lead Norway and Denmark, Oncology MScPharm. Title: Breakthroughs that change people's lives.
- PubGene by **Håvard Hildeng Hauge**, Board member, PhD. Title: Enabling personalized medicine – putting patients first.
- SINTEF by **Hanne Haslene-Hox**, PhD, Research Scientist. Title: High-throughput screening, analysis and biopharma ceutical production for cancer therapy.



18.09.19 // Do human cancer cell lines really behave in the same way as clinical tumor material? Professor Bruce Baguley, University of Auckland, Auckland Cancer Society Research Centre, New Zealand.

In this CCBIO Special Seminar, Professor Baguley explained how cancer cell lines have emerged as one of the main laboratory tools for the investigation of cancer behavior and of response to therapy. His group wanted to compare the behavior of cell lines with that of short-term cultures of clinical material taken during cancer surgery. He discussed the results of their study in terms of a model in which tumors contain two major populations, one in which proliferation is controlled mainly by a cell cycle restriction point, and one in which cell loss is controlled by an axis that links apoptotic tumor cells, the AXL receptor, and macrophages. The main conclusion is that the proportion of these two populations may fluctuate with time, with important implications for cancer therapy.

04.10.19 // Clinical trials in the future. This CCBIO Mini-Symposium focused on the topic of clinical trials in the future, inviting the audience to glance into the future and view coming trends, including next generation technology and artificial intelligence. This session was an integrated part of the new CCBIO course Clinical Trials in Cancer Research, opened up to a larger audience in a CCBIO Mini-Symposium.

Speakers included:

- **Fredrik Öhrn**, Gothenburg. Title: Design of clini cal trials in the future.
- **Tove Skjelbakken**, Tromsø. Title: Desicion aids.
- **Donal Landers**, Manchester. Title: Digital experimental medicine in oncology.
- **Ketil Widerberg**, Oslo. Title: How artificial intelligence can improve clinical trials.

12.12.19 // Metastatic Latency - Models and Mechanisms. Srinivas Malladi from the Department of Pathology, UT Southwestern, Dallas. CCBIO Special Seminar.

Dr. Malladi's lab is focused on understanding how disseminated cancer cells survive and give rise to overt metastasis at a cellular and molecular level using a multidisciplinary and integrative approach. He explained how metastasis frequently develops years after the removal of a primary tumor, from a minority of disseminated cancer cells that survived as latent entities through unknown mechanisms. His group isolated latency competent cancer (LCC) cells from early stage lung, breast and kidney cancer cell lines and defined the mechanisms that suppress outgrowth, support long-term survival, and maintain tumor-initiating potential in these cells during the latent metastasis stage. Breast and lung adenocarcinoma LCC cells are enriched for SOX family transcription factors and self-impose a slow-cycling state by expressing WNT inhibitor DKK1. Slow-cycling LCC cells downregulate NK cell activating ULBP ligands and evade NK-cell-mediated clearance. Comparative examination of LCCs and their metastatic counterparts reveal distinct signaling and metabolic circuits in LCC cells. Dr. Malladi explained how his group is systematically investigating the molecular and cellular determinants of metastatic latency in these models to reveal new vulnerabilities that can be targeted to eliminate LCC cells. ••

The 7th CCBIO Annual Symposium 2019

May 13-14, 2019 at Solstrand Hotel & Bad

For the 7th time, CCBIO invited researchers to the CCBIO Annual Symposium at Solstrand Hotel close to Bergen, Norway. Top scientists from all over the world gathered to discuss recent advances in cancer research with the 200 conference participants. Yet again, the otherwise unstable Norwegian spring weather showed itself at its best. And as before, a broad range of presentations should provide something to learn and bring home for everyone in the audience, and for the CCBIO research groups as well. This year, topics ranged from calculating the risk of breast cancer through genetic tests, to drug development and innovation.

Keynote speaker on the innovation session, **Professor Omid Farokhzad** from Harvard Medical School, was concerned with turning academic innovations into medical products and technologies with great impact on lives and society. He encouraged the audience to make their ideas come to life: They should go after solving important and big problems. If they do so, usually the scientific community rewards them with a high impact publication, providing validation in a peer reviewed process. They should also protect their innovation by filing patents before publicly disclosing the findings, a prerequisite for getting investors interested in their ideas and add the capital they need to advance their ideas and concepts further. He still pointed out that academic ideas are inherently risky, and that a majority of them will fail. Investors however know that this is risk capital with a chance of failure, but also with a chance of being enormously successful, exceeding the losses in the long run.

In his closing remarks, **Roger Strand** suggested that concepts of balance and nuance characterized many of the sessions. He found that the individual presentations all offered novel contributions in terms of methods and results, but most presenters also emphasized the size of the challenges that we are faced with. For every gene or signaling pathway identified in a particular cancer, it seems that we also learn ever more about the almost endless variation, heterogeneity and biological complexity manifested by that cancer.

Marta Bertolaso summarized this in her presentation "Models and explanations in cancer research" as "a problem of perspective, and not a problem of getting more data". In this sense, CCBIO and its symposia offer opportunities for intellectual exchange that may contribute to our scientific understanding of cancer.

The poster sessions have become a popular attraction during the symposia, this year with 41 posters and 53 poster presenters. As the posters covered a broad range of cancer research, two poster committees were appointed from CCBIO's international affiliated researchers. One for basic medical research posters (Randy Watnick and Arne Östman) and one for clinical research posters (Hani Gabra and Ian Mills). The two winning posters in the category of basic medical research were presented by Wenjing Zhou and Kjersti Davidsen, Sturla Magnus Grøndal and Noelly Madeleine. The two winners in the category of clinical research were Magnus Blø and Havjin Jacob.

In 2020, the Annual Symposium will take place May 12-13, and in 2021 on May 19-20. ••

Centre for Cancer Biomarkers

7th CCBIO Symposium 2019

Solstrand, May 13-14, 2019, Bergen, Norway

SCIENTIFIC PROGRAM

Day 1: Monday May 13, 2019

09:00-10:00	**Registration and Coffee**
10:00-10:15	Lars A. Akslen (Director of CCBIO): Introduction to CCBIO Symposium 2019
	Chair: Bjørn Tore Gjertsen
10:15-11:00	Bob Löwenberg: Directions in the treatment of acute myeloid leukemia
11:00-11:45	William D. Foulkes: How do we identify those at risk for hereditary cancer?
11:45-12:30	Vicky Seewaldt: Systems biology approach to improve survival of Black and Latina women with biologically aggressive breast cancer
12:30-14:30	**Lunch and poster session I**
	Chair: Mark LaBarge
14:30-15:15	Jonathan Irish: Hacking the signals that control cell identity using single cell mass cytometry
15:15-15:45	Nick Tobin: Assessing the clinical relevance of gene expression signatures in primary and metastatic breast cancer
15:45-16:15	Xisong Ke: Discovery and target identification of anti-cancer drugs
16:15-16:45	**Coffee break**
	Chair: Roger Strand
16:45-17:45	Eirik Tranvåg & Roger Strand: Which patient to treat? An interactive priority setting survey
19.30	**Dinner**

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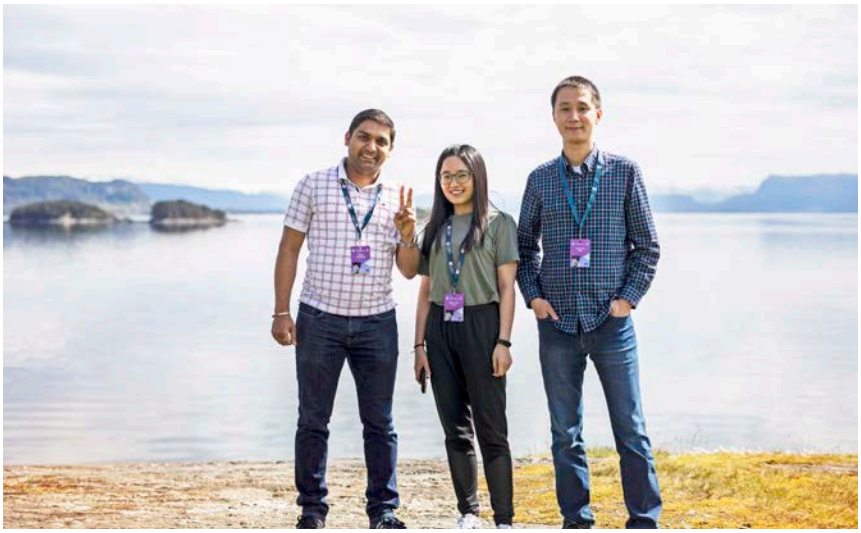
CENTRE FOR DIGITAL LIFE NORWAY

Day 2: Tuesday May 14, 2019

	Chair: Jean Paul Thiery
09:00-09:45	Randy Watnick: Development of a therapeutic peptide that reprograms the tumor immune microenvironment
09:45-10:30	Duanqing Pei:New strategies and molecular insight in cellular reprogramming
10:30-11:00	**Coffee break**
	Chair: Ian Mills
11:00-11:30	Eric B. Haura: Visualizing protein complexes as molecular diagnostics
11:30-12:00	Agnete Engelsen: Microenvironment-induced AXL signaling is required for epithelial phenotypic plasticity
12:00-12:30	Alea Mills: Strengths & vulnerabilities of human glioma
12:30-13:00	Caroline Heckman: Bone marrow stroma derived factors and other mechanisms of resistance to therapy in hematological malignancies
13:00-14:45	**Lunch and poster session II**
	Philosophy of Cancer *Chair: Roger Strand*
14:45-15:15	Marta Bertolaso: Models and explanations in cancer research
	Translation & Innovation *Chair: Yves Aubert*
15:15-15:30	Yves Aubert: Creating impact through innovation
15:30-16:30	Volterra Lecture by Omid Farokhzad: Perspectives on how to translate bio-medical research to products and cures.
	The session was sponsored by CCBIO, Digital Life Norway, VIS, and The Faculty of Medicine UIB.
16:30-16:45	Roger Strand (CCBIO PI): Closing remarks

The 7th Annual Symposium

May 13-14, 2019
at Solstrand Hotel & Bad




International Collaborators


Dan Crichton, PhD
- Big Data
Caltech
Ashish Mahabal, PhD
- Image analysis, integr.
Lars Grimm, MD
- Breast Imaging
Joseph Geradts, MD - Pathology
Data Validation, Annotating, Archiving, Integration
Caltech


enerative Epithelial Stem Cells by
led with Imaging Mass Cytometry


Results


Where are we going?

Opening Symposium for the Hyperion Imaging System

February 6, 2019 at the Haukeland University Hospital & University of Bergen

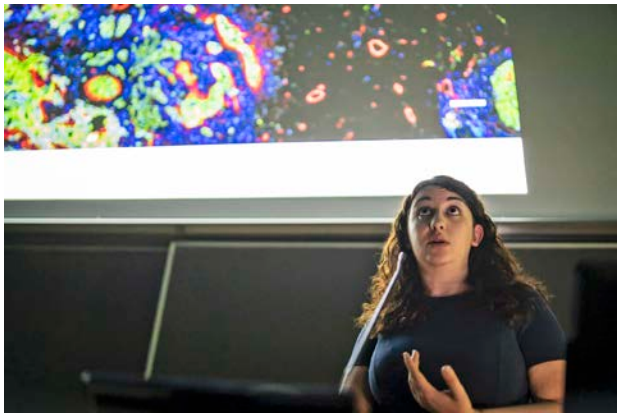
The Hyperion Imaging System is the next generation immunohistochemistry where researchers can explore tissue biology with 35 antibodies simultaneously. The seminar provided an introduction to the research possibilities offered by the Hyperion Imaging System and examples of ground-breaking research. **Leigh-Anne McDuffus** from the Fluidigm Corporation explained the features of the Hyperion Imaging System. Keynote speaker was **Dr. Dario Bressan**, Head of the IMAXT Laboratory, CRUK Cambridge Institute, University of Cambridge, UK, who showed many examples from his own research. Management representatives of CCBIO, the Medical Faculty and Helse Bergen gave talks on the possibilities, the practicalities and the availability of the Hyperion. **Sveinung Hole**, CEO of the Trond Mohn Foundation, made a presentation that put the Hyperion Imaging System into the context of the Trond Mohn Foundation's overall strategy.

CCBIO is the owner of the new instrument that was financed by a consortium of CCBIO, the Faculty of Medicine and the Bergen Research Foundation (BFS). Access to the equipment is managed and operated by the Flow Cytometry Core Facility. When established, this multiplexing tissue analyzer was the only one of its kind in Northern Europe, and it is available for use by both national and international researchers.

The Hyperion Imaging platform is combining two modules: the Hyperion Tissue Imager and a Helios CyTOF® system. The Helios/Hyperion system use metal tagged antibodies towards specific proteins of interest in select regions of fixed tissue sections, frozen tissue section or cell smears or cell suspension samples.

This technology utilizes a state-of-the-art Time-of-Flight Inductively Coupled Plasma mass spectrometry technology together with elemental tags that have higher molecular weights than those elements that are naturally abundant in biological systems.

The advantage with using mass cytometry on cells in suspension is that it does not produce the same overlap as when using fluorochromes in flow cytometry, and thus there is little need for compensation. No fluorescence background also makes this technology very suitable for looking at high dimensional functional and phenotypic correlations at single cell level, accelerating biomarker findings and developing targeted drug therapy (precision medicine).



The Hyperion Imaging System provides a visual context to the heterogeneity of tissue landscapes that we have not been able to do before. This is possible because of the up to 35-40 metal tags used to simultaneously detect multiple proteins on one tissue section, which allows for understanding of protein behaviors and interactions to drive biological breakthroughs and define clinical biomarkers.

Or very short said, as key speaker Dr. Dario Bressan used as an analogue, consider it a "google map" for tumors. ••

Centre for Cancer Biomarkers

OPENING SYMPOSIUM FOR THE HYPERION IMAGING SYSTEM February 6, 2019

Auditorium 1, BB-building, Haukeland University Hospital & University of Bergen

Chair: Sonia Gavasso

13:00	Introduction: Lars A. Akslen, Director, CCBIO Marit Bakke, Vice Dean, Faculty of Medicine Kjell Morten Myhr, Head of Department, Department of Clinical Medicine Sveinung Hole, CEO of the Trond Mohn Foundation
13:15	The core facility concept & procedures for access: Geir Olav Løken, Administrative Leader, CCBIO Silke Appel, Platform Leader, FLOW
13:30	The Hyperion Imaging System: Leigh-Anne McDuffus, Fluidigm Corporation
14:15	Keynote lecture: Dr. Dario Bressan, University of Cambridge
15:15	Mingling session with tapas

Satellite Symposium on Deep Tissue Profiling

May 12, 2019 at Solstrand Hotel & Bad

Since 2018, CCBIO has arranged an annual satellite symposium in connection with the CCBIO Annual Symposium. In 2019, the overarching topic was Deep Tissue Profiling and attracted 70 participants in an international blend, many of which stayed on for the main CCBIO Annual Symposium 2019. CCBIO is scientifically responsible for the Hyperion Imaging System, and Senior Researcher **Sonia Gavasso** chaired the meeting and also did the closing remarks. **Kurt Schalper** discussed the "window of opportunity for immune therapy" and the importance of functional markers to identify the responsive state of immune cells within tumors. **Hamid Raza Ali** exemplified complex data analysis at the single cell level of tumor ecosystems and the implications of cellular states and microenvironments to align tumor biology with therapeutic interventions to advance precision oncology. Vision, technology and action are deep-rooted in CCBIO, and the satellite symposium proved a perfect arena for inspiration to further our understanding of tumor biology.

The satellite symposium took up the important discussion of the significance of tissue context and topography. Such information is needed to advance the field of omics studies, e.g. through techniques such as imaging mass cytometry. Equally important are the intense discussions and networking which took place during this meeting. Lively discussions ensued on neighborhoods within tumors in terms of ecosystems, microenvironments, immunology, "crime scenes", patterns, segmentation and data analyses. Hence,

Gavasso found that adopting concepts from other disciplines to understand complex tumor biology became a central theme at the CCBIO Satellite Symposium. The good vibrations continued throughout the main symposium, making it a privilege for CCBIO to host such outstanding scientists.

In 2020, the Satellite Symposium will take place on May 11, and focus on *Biomarkers in Immunotherapy.*••

Centre for Cancer Biomarkers

CCBIO SATELLITE SYMPOSIUM ON DEEP TISSUE PROFILING May 12, 2019

Solstrand, Bergen, Norway

SCIENTIFIC PROGRAM

10:00-12:00	Registration
12:00-13:00	**Lunch**
13:00-13:15	Lars A. Akslen (Director of CCBIO): Introduction and Opening words
	Chair: Jim Lorens
13:15-13:45	Kurt Schalper: Understanding the immune composition of human lung cancer using multiparametric and spatially resolved tissue analysis
13:45-14:15	Harris Fienberg: High fidelity multiplexed imaging
14:15-14:45	Teijo Pellinen: Multiplexed IHC reveals fibroblast subtypes with outcome and gene mutation correlations in prostate and lung cancer
14:45-15:15	Carina Strell: Placing RNA in context and space - methods for spatially resolving transcriptomics
15:15-15:45	**Break with coffee and refreshments**
	Chair: Sonia Gavasso
15:45-16:15	Jonathan Irish: High dimensional single cell analysis of human blood, tissues, and tumors
16:15-16:45	Artur Mezheyeuski: The in situ immune profiling of solid tumors
16:45-17:15	Hamid Raza Ali: Sculpting of tissue phenotype by the somatic breast cancer genome
17:15-17:30	Sonia Gavasso: Closing words
19:00	**Dinner**

INTPART: Iceland Research Meeting with Stimulating Scientific Eruptions

August 29 - September 2, 2019, Reykjavik, Iceland

As part of the CCBIO - VBP ongoing INTPART project, "Bergen-Harvard Cancer Studies: A Partnership for Excellent Education and Research", scientists and students from CCBIO and Harvard Medical School, the Vascular Biology Program (VBP), met "in the middle" between Boston and Bergen, in Reykjavik, Iceland.

Focus on interaction

The organizers, **Elisabeth Wik** and **Assistant Professor Michael Rogers** (VBP), backed up by the initiators and project directors **Lars A. Akslen**, **Roger Strand**, and **Professor Marsha A. Moses,** Director of the VBP at Boston Children's Hospital, wanted this meeting to enable cross-fertilization and to generate ideas and action plans for new collaborations. Inspired by Iceland's dramatic landscape, Akslen expressed a hope that the 45 participants should be stimulated to scientific eruptions.

Getting an overview of each other's research

The first two days consisted mainly of 5 minutes' project presentations and pitches from most participants. These were meant to introduce interests, resources, and skills to the group so that attendants could find overlapping or complementary areas suitable for collaboration. All were asked to form their talks to generate interest for interaction. The details were then discussed in ad hoc meetings or over meals during four full days.

Inspirational lectures

Besides short project presentations, the scientific program consisted of lectures and workshops on a range of different topics, aimed to give inspiration, provide food for thought, show common grounds and differences, and hopefully provide new ideas.

Professor Bruce Zetter from the VBP set the scene telling the "saga of the epithelial cell". His very vivid lecture was an exercise in how to give a research presentation to remember, communicating the story of your work. **Robert D'Amato** from the VBP shared his career story and the results of scientific curiosity, dedication and persistence. The D'Amato lab

discovered that the drug Thalidomide was a potent inhibitor of angiogenesis, leading to repurposing for blood born cancers and multiple myeloma therapy. VBP's **Randy Watnick** told the story of his research path, including examples of collaborations and new ideas, hard work, obstacles, challenges and motivation, all the way to the foundation of a company. A pioneer in 3D organoid modeling, **Amir Aref** from the Dana-Farber Cancer Institute at Harvard Medical School, showed intriguing technology which captures the patient's own tumor microenvironment on microfluidic chips as 3D cultures, for the efficient testing of immuno-oncology therapeutics. From CCBIO, among others PhD candidate **Hanna Dillekås** provided inspiration, with the history of breast cancer - and how politics have influenced it.

Different and new approaches

Inspiration might also come from other ways of doing things. VBP's **Mike Rogers** gave an interesting overview of the learning methods used at Harvard Medical School. Traditional auditorium lectures are now only used for core material, as Active Learning has proved a much more productive learning method. This is problem-based learning, which shares benefits with case-based collaborative learning (CBCL). **Diane Bielenberg** and **Roopali Roy**, both from the VBP, gave a breakdown of the US mentoring system, to which Norway has no equivalent. "Build your own set of mentors regardless of formal organization, and take responsibility of your own learning," they urged.

Societal considerations

The meeting included a variety of sessions devoted to ethical and societal aspects of cancer research, organized by CCBIO's team for Ethical, Legal and Social Aspects (ELSA). Indeed, almost a third of the meeting participants were affiliated with this program, including economists, social scientists, philosophers, ethicists and theoretically inclined cancer researchers. According to **Roger Strand**, "a major accomplishment for CCBIO, which makes it almost unique on a global basis, is that we have observed increasing integration and convergence between biomedical, ethical and societal aspects." In CCBIO, ELSA-related activities are no longer specialist add-ons. Rather, they have become an intrinsic part of CCBIO as a research endeavor and of the Boston-Bergen collaboration.

Any eruptions yet?

In summary, the INTPART CCBIO-VBP meeting enabled consolidation of previously initiated project collaborations, new partnerships came into play, students and junior researchers got to know each other and learned from each other's and the senior researcher's experiences. We are confident that seeds for future collaborations were sown and that this gathering was a suitable soil. The educational sessions also added to the meeting's excellence, providing lectures on topics not presented elsewhere in Norway. Our younger participants clearly felt they came enriched from the Iceland meeting, as you can read in an interview with some of them in the full report from the meeting. The meeting received excellent evaluations in the anonymous post-meeting survey. **Elisabeth Wik**, CCBIO's INTPART coordinator concluded: "This was a true CCBIO-VBP collaborative effort, a major part of what we wanted to accomplish through the INTPART Phase-1 project." ••

Full report from the meeting →

Centre for Cancer Biomarkers

CCBIO-VBP Research Meeting

August 29 – September 2, 2019, Reykjavik, Iceland

Meeting organizers: Elisabeth Wik and Michael Rogers

Thursday August 29

18:00-19:30 Get-together

19:30 Dinner

Friday August 30

09:00-09:30 Welcome: Lars A. Akslen, Elisabeth Wik, Michael Rogers, Roger Strand

09:30-10:15 Bruce Zetter: The story of cancer, and how to tell your own research story

10:15-10:45 Coffee break

10:45-11:30 Project introductions, session 1:
- Elisabeth Wik: Breast cancer of the young; a unique biology?
- Ulrikke Hugaas: Molecular breast cancer subtypes; heterogeneity across primary tumor and metastatic lesion in breast cancer of the young?
- Danielle Sim: Functional characterization of cancer stem cells in pancreatic and ovarian cancer
- Eirik Tranvåg: Cancer biomarkers for better (or for worse) priority setting
- John Cairns: Learning when to say no

11:30-11:45 Coffee break

11:45-12:30 Project introductions, session 2:
- Michael Rogers: Identifying and validating new drug targets for angiogenesis-dependent diseases
- Aram Ghalali: AZIN1 as a potential therapeutic target in human cancers
- Ridhima Das: Isolation and characterization of cells derived from human epithelial rests of Malassez
- Caroline B. N. Engen: Exploring the boundaries of precision hemato-oncology - The case of FLT3 length mutated acute myeloid leukemia
- Mille S. Stenmarck: Reframing cancer
- Diana Siyam: Identifying the key mediators of the interaction between mesenchymal stem cells derived from oral fibroblasts and oral cancer microenvironment
- Yang Lee: Promoting lymphangiogenesis to protect obesity

12:30-14:00 Lunch break

14:00-14:45 Project introductions, session 3:
- Ingunn Stefansson: Loss of androgen receptor expression is associated with aggressive tumor features and reduced survival in breast cancer patients
- Amalie Tegnander: AGR2 and AGR3 in primary breast cancer: part of the ER-related cancer biology?
- Kenneth Finne: Proteomic characterization of tumor cells and tumor microenvironment in breast cancer
- Hanna Dillekås: Importance of tissue trauma and wound healing on escape from tumor dormancy
- Golnaz Morad: The role of breast cancer-derived extracellular vesicles in brain metastasis
- Agnete Engelsen: Microenvironment-induced AXL signaling is required for epithelial phenotypic plasticity of normal and malignant epithelial cells

14:45-15:00 Coffee break

15:00-15:45 Project introductions, session 4:
- Astrid Børretzen: Epithelial-mesenchymal plasticity and microvascular proliferation in aggressive prostate cancer
- Andrej Jedinak: Benign prostate hyperplasia vs. prostate cancer: potential therapeutic targets and biomarker discovery
- Maria Lotsberg: High-dimensional analysis of the tumor microenvironment
- Austin Rayford: Elucidating the role of AXL in cellular plasticity
- Harsh Dongre: Tumor-stroma crosstalk in vulva squamous cell carcinoma
- Cornelia Schuster: Impact of stress response in melanoma treatment
- Daniela Costea: Tumor-stroma (CAFs) interactions in head and neck & vulva squamous carcinoma
- Katie Fehnel: Axon guidance factors in cerebral cavernous malformations

15:45-16:00 Break with coffee and refreshments

16:00-16:45 Robert D'Amato: From Thalidomide to Pomalyst, a 50 year journey

19:30 Dinner

SCIENTIFIC PROGRAM

Saturday August 31

09:00-10:00 Roopali Roy: Proteases in vascular biology and cancer

10:00-10:30 Coffee break

10:30-11:00 Hanna Dillekås: The history of breast cancer - and how politics have influenced it

11:00-11:30 Yves Aubert: Moving the goal posts of scientific research: from publication to societal impact

11:30-11:45 Coffee break

11:45-12:30 Parallel sessions and ad hoc project meetings

- 11:45-12:30: Amir Aref: Patient derived organoids in cancer research
- 11:45-12:30: ELSA team: Uncertainty in medicine

12:30-14:00 Lunch break

14:00-15:30 Parallel sessions and ad hoc project meetings

- 14:00-14:45: Yves Aubert: Understanding the role of innovation in research grant proposals
- 14:45-15:30: Kenneth Finne and Austin Rayford: Imaging mass cytometry - Getting to know the Hyperion
- 14:00-15:30: ELSA team: Reframing cancer

15:30-16:00 Coffee break

16:00-17:00 Randy Watnick: The trials and tribulations of translational research

20:00 Dinner

Sunday September 1

09:00-17:00 Sightseeing by bus: Þingvellir, Lake Þingvallavatn, geysir Strokkur, Gullfoss.

18:15-19:15 Marta Bertolaso and Roger Strand: The role of cells versus tissues in cancer: a philosophical approach

19.30 Dinner

Monday September 2

09:00-09:45 John Cairns: Sunshine mixed with a little hurricane: the perfect storm that is the economic evaluation of targeted cancer therapies

09:45-10:15 Coffee break

10:15-11:15 Parallel sessions and ad hoc project meetings

- 10:15-11:15: Michael Rogers: Case-based collaborative learning (the CBCL method)
- 10:15-11:30: ELSA team: What is a good biomarker?

11:15-11:30 Coffee break

11:30-12:15 Diane Bielenberg and Roopali Roy: Structured mentoring: Bridging the mentor—mentee gap

12:30-14:00 Lunch break

14:00-15:30 Parallel sessions and ad hoc project meetings

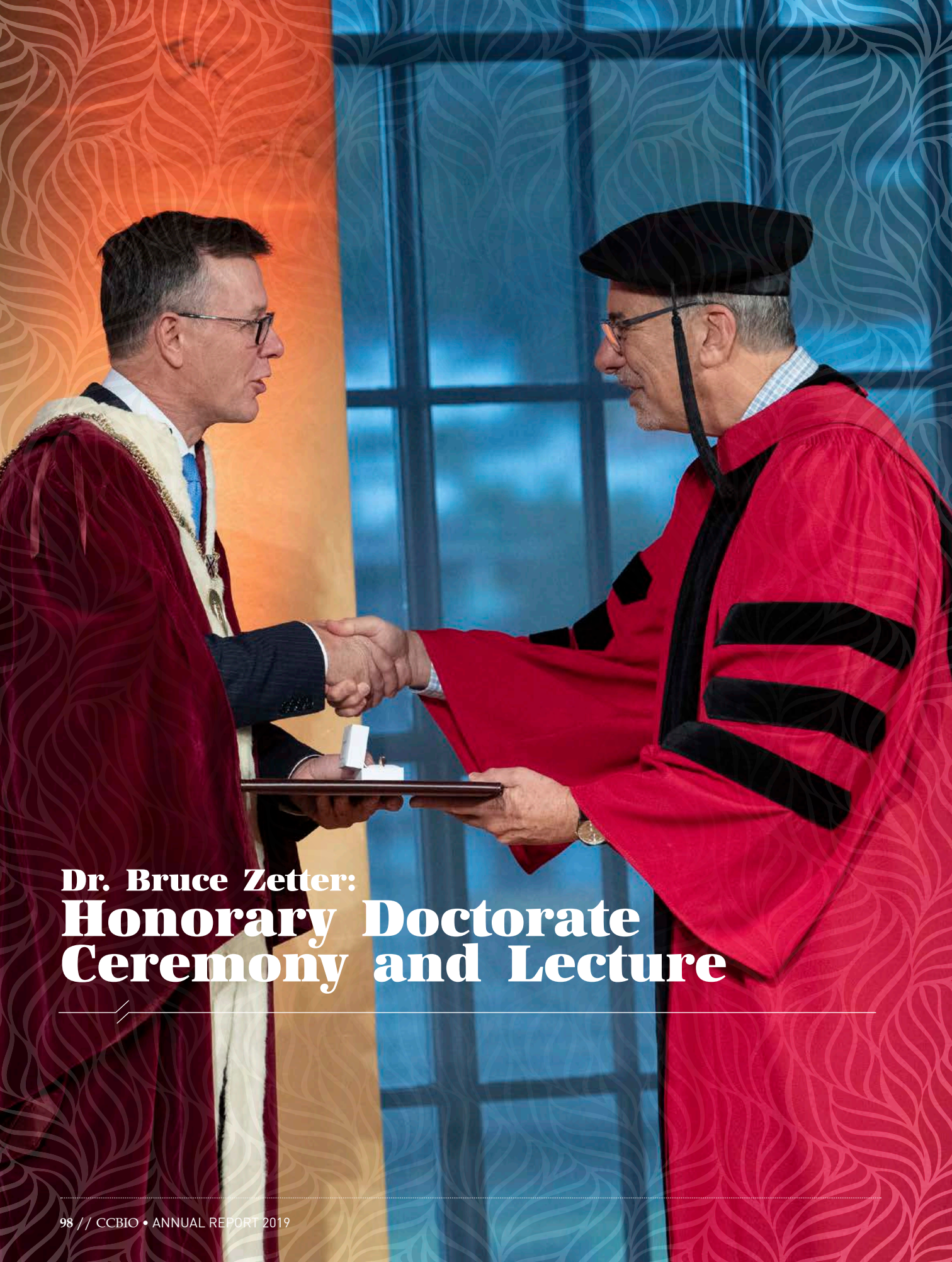
- 14:00-14:45: Golnaz Morad: Extracellular vesicles in human pathologies
- 14:45-15:30: Yang Lee: In vivo lymph transport measurement
- 14:00-15:30: ELSA team: How real-world evidence has been used in the evaluation of cancer drugs

15:30-16:00 Coffee break

16:00-17:00 Michael Rogers: Metastases without cancer

17:00-17:30 Elisabeth Wik and Michael Rogers: Feedback and sum-up

19:30 Dinner



Dr. Bruce Zetter:
Honorary Doctorate Ceremony and Lecture

October 14, 2019
in Store Auditorium, Haukeland University Hospital

October 15, 2019
in the University Museum Aula, University of Bergen

October 15, **Professor Bruce R. Zetter** from Harvard Medical School and Boston Children's Hospital was appointed as Honorary Doctor at the University of Bergen, Faculty of Medicine. October 14, he gave his honorary doctor lecture, on the topic "*RNA as a tool for cancer therapy*". The day before the Honorary Doctor Ceremony, the University Museum had its grand opening after 6 years of renovation, with the opening speech by Prime Minister **Erna Solberg**, backed up by Minister of Research and Higher Education **Iselin Nybø**, Minister of Local Government and Modernisation **Monica Mæland**, the Bergen Mayor **Marte Mjøs Persen**, the University Rector **Dag Rune Olsen** and the Museum Director **Henrik von Achen**. The new honorary doctorates attended the opening ceremony as honorary guests from the VIP stands together with the ministers and their entourage.

In his Honorary Doctor lecture, attended by an overfilled auditorium with more than 270 participants, Dr. Zetter talked about how the treatment of cancer has seen dramatic improvements in the last decade, yet many patients still fail to respond to current therapies. Most currently used cancer drugs are small chemical molecules that antagonize cancer pathways, yet many cancer-promoting pathways do not respond to these agents. The delivery of RNA molecules to tumors provides a new way to target some of these previously "undruggable" targets. Dr. Zetter described new advances in RNA drug delivery to tumors that both disable cancer-promoting genes and also restore the activity of natural tumor-suppressor genes. This double punch to the cancer cell can provide dramatic anti-tumor effects in experimental animals and, hopefully, in human patients.

On October 15, the Honorary Doctorate conferment ceremony was carried out in the Museum Aula. The honorary doctors and UiB notabilities entered with pomp and circumstance and speeches were held by amongst others UiB's Rector **Dag Rune Olsen** and the deans from all faculties as well as **Sir Peter Gluckman**, the latter on behalf of the Honorary Doctors.

It was a great honor for CCBIO and The Medical Faculty to be awarded this honorary doctorate. In CCBIO's nomination, we commend Dr. Zetter's 40 years in cancer research, and consider him a pioneer in the fields of tumor angiogenesis and cancer metastasis. Working closely with Dr. Judah Folkman in the Vascular Biology Program (VBP) at Boston Children's Hospital, Dr. Zetter is credited with defining the role of cell migration in the development of metastatic cancers, developing novel biomarkers to predict patient outcomes, and developing new therapies for vascular malformations and for treating aggressive cancers. Noted for his creativity, Dr. Zetter's writings and lectures have dramatically changed the thinking of the cancer research community. In addition to his research accomplishments, Dr. Zetter has served as the Chief Scientific Officer and Vice President for Research at Boston Children's Hospital and is an advisor to numerous biotechnology companies and academic institutions worldwide, notably including CCBIO. Here, he is a member of the CCBIO Scientific Advisory Board, and also an important contributor in the CCBIO-VBP INTPART collaboration. ••

4th Scandinavian Seminar on Translational Pathology

October 23-24, 2019 at Solstrand Hotel & Bad

SCANPATH is a CCBIO-initiated annual network meeting for Scandinavian tumor pathologists and pre-clinical scientists with an interest in the prospects of next generation tissue profiling. The aim is to stimulate tissue-based studies of tumor mechanisms and biomarker mapping. This meeting has been a success since the startup in 2016 and is now a well-established annual forum held also in Sigtuna, Sweden (2017) and Gustavelund, Tuusula, Finland (2018), before coming back to Bergen (Solstrand) in 2019.

The scientific program of this year's Translational Pathology Seminar was filled with inspirational and educational presentations and included internationally renowned researchers. Among others, **Fredrik Pontén** provided an update to the Human Protein Atlas, and their continued efforts to characterize the human proteome. **Karin Jirström** gave us her thoughts on the future of pathology, emphasizing the emerging need for pathologists in therapy decisions. **Teijo Pellinen** demonstrated intriguing methods for characterizing the cancer microenvironment by multiplex immunofluorescence, and **Elisabeth Wik** presented two interconnected stories about nerve infiltration in breast cancer, and breast cancer in the young. The program also gave room for several local PhD students to present their inspiring work, including **Astrid Børretzen**, **Cecilie Askeland**, **Hilde Engerud** and **Anna Sæle**.

Moreover, the participants enjoyed an informal and highly engaging "Posters & Prosecco" session with 14 attending posters. The Seminar and poster session were further enriched by presentations and stands from our industry partners **Aiforia, Bayer**, **Fluidigm**, **NanoString Technologies** and **Roche Diagnostics**.

CCBIO's Director **Lars A. Akslen** found this year's Translational Pathology Seminar to have been a very stimulating meeting with a firm focus on spatial resolution and attempts to integrate tissue context with various omics data. Some of the presentations and recent developments in morphology-based techniques, such as imaging mass cytometry, reminded him of the excitement at the time when the Hubble telescope was introduced in modern

cosmology. "Now it's up to us to continue our "Hubble approach" in studies of tissue landscapes in tumors and other diseases", he commented.

Next year's seminar will be held in Lund, Sweden, November 27-28, 2020. ••

Centre for Cancer Biomarkers

4th Scandinavian Seminar on Translational Pathology

Solstrand, October 23-24, 2019, Bergen, Norway

	Day 1: Wednesday October 23, 2019
09:00-10:00	**Registration and Coffee**
10:00-10:15	Welcome and Introduction: Lars A. Akslen & Arne Östman
	Chair session 1: Elisabeth Wik
10:15-10:45	Karin Jirström: Therapeutic pathology: time to move on
10:45-10:57	Astrid Børretzen: Epithelial mesenchymal plasticity in aggressive prostate cancer
10:57-11:09	Cecilie Askeland: Stathmin expression associates with BRCA1 germline mutations, a basal-like phenotype and features of aggressive breast cancer
11:09-11:21	Max Backman: Concepts of immunity in cancer: oases in the desert
11:21-11:33	Hilde Engerud: PDL1 and PD1 expression in endometrial cancer
11:33-11:45	Anna Sæle: GATA3 expression in relation to immune response and aggressive breast cancer phenotypes
11:45-11:57	Marc Rassy: Can routine next generation sequencing help favour a specific tumor origin?
11:57-12:12	Company presentation by Roche Diagnostics: Claire Faure: Precision medicine for cancer patients: technologies to leverage the increasing expertise of pathologists
12:15-13:30	**Lunch break**
	Chair session 2: Carina Strell
13:30-14:00	Teijo Pellinen: Multiplexed imaging of the tumour microenvironment
14:00-14:15	Marius Lund-Iversen: Correlation between serum levels and tissue expression of proGRP
14:15-14:30	Olga Surova: In situ sequencing for visualization of tumor heterogeneity

SCIENTIFIC PROGRAM

14:30-14:45	Kenneth Finne: Distinct hypoxia response in luminal-like and basal-like breast cancer
14:45-15:00	Artur Mezheyeuski: Immune landscape in colon and rectal cancers
15:00-15:15	Company presentation by Nanostring: Lene Berlick: GeoMxTM Digital Spatial Profiler Morphological context and high-plex protein or RNA expression data – now possible from just one FFPE slide
15:15-15:45	**Coffee & Crosstalk**
	Chair session 3: Reidunn Edelmann
15:45-16:00	Björn Gylling: Cachexia, sarcopenia and infiltration of CD3+ and CD8+ T-lymphocytes in CRC
16:00-16:15	Mercedes Herrera Torres: Fibroblast heterogeneity in CRC
16:15-16:30	Carina Strell: Stromal PDGFRb as predictive marker for benefit from postoperative radiotherapy in ductal carcinoma in situ and early stage invasive breast cancer
16:30-16:45	Johanna Arola: Nation-wide cohort of rare tumor collected from hospital biobanks
16:45-17:00	Marit Valla: Artificial intelligence in pathology
17:00-17:15	Sverre Torp: ErbB receptor expression in human meningiomas
17:15-17:30	Elin Richardsen: MicroRNAs in prostate cancer - a multicenter study
17:30-17:45	Company presentation by Aiforia: Sami Blom: Deep Learning image analysis for pathology without the need of coding or data science
18:15-19:15	**Posters & Prosecco**
19:15	**Dinner**

Day 2: Thursday October 24, 2019

	Chair session 4: Kenneth Finne
09:00-09:30	Fredrik Pontén: The Human Protein Atlas - implications for human biology and precision medicine
09:30-09:45	Cecilia Lindskog: Integrated omics for single cell analysis
09:45-10:00	Roberta Lugano: CD93 - a key player in glioma vascular biology
10:00-10:15	Xinsong Chen: Patient-derived whole-tumor cell culture as a platform for breast cancer therapy response prediction
10:15-10:30	Guttorm Haraldsen: Single-cell RNA-Seq and therapeutic resistance in auto immune disease
10:30-11:00	**Coffee & Crosstalk**
	Chair session 5: Patrick Micke
11:00-11:30	Elisabeth Wik: Two stories: Nerves and vasculature in breast cancer, and breast cancer of the young
11:30-11:45	Balazs Acs: Artificial intelligence as the next step towards precision pathology
11:45-12:00	Sebastian Lundgren: Quantitative, qualitative and spatial analysis of the immune landscape in periampullary and pancreatic adenocarcinoma
12:00-12:05	Monica Nistér: The Swedish childhood tumor biobank – an update
12:05-12:20	Maxime Garcia: Sarek, a workflow to detect germline and somatic mutations in WGS/WES
12:20-12:35	Company presentation by Fluidigm: Olga Karpus: Imaging Mass Cytometry (IMC): highly multiplexed antibody-based technology with subcellular resolution
12:35-12:40	Closing remarks
12:40-13:30	**Lunch & Goodbye**


Dissemination
and Communication
2019

Dissemination and Communication

CCBIO aims to disseminate and communicate 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 keeps its webpages updated at all times, presenting various news stories from our research community, and ensuring that our numerous open events are well advertised.

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 and Twitter accounts, and encourages our researchers and students to promote their research and activities through the social media as well, using the tag #ccbio.

Examples of Facebook entries:

Video of Professor Bruce Zetter from his Honorary Doctor lecture, giving 3 tips to students on how to achieve success as a cancer researcher.

Facebook entry with a video providing glimpses from the CCBIO Annual Symposium 2019.

Examples of Twitter entries:

Interview with Professor Lars A. Akslen on a research project showing that 3D mammography does not detect more cancer. It is however more accurate than traditional mammography. Paper published in Lancet Oncology. (Hofvind et al., 2019.)

Twitter entry on the opening symposium of the Hyperion Imaging System, stating that this new technology acquired by the Medical Faculty and CCBIO facilitates more top-notch research.

Popular Science Enacted

CCBIO has a dissemination effort aimed especially at children and youths in collaboration with the actor and cancer researcher Henriette Christie Ertsås, a CCBIO alumna. She offers performances and lectures on cancer and biomarkers to schools on CCBIO's behalf. Schools have a choice between the play "Stop the cancer cell Gloria Glutton!" appropriate for children aged 4 to 13, the lecture or stand-up routine "Christine the Cancer Cell - A sociopath in the body," suitable for youth and adults and the play "Stine Stem Cell finds herself", for children aged 9 to 15. All are free of charge for schools.

Henriette is an important part of the CCBIO stand at the Research Fair ("Forskningstorget"), creating quite an attraction.

"Stine Stem Cell finds herself" was particularly popular in 2019. It is a free-standing drama adaptation of the book "*Biomarkers of the Tumor Microenvironment: Basic Studies and Practical Applications*" by Lars A. Akslen and Randolph Watnick (editors). Stine Stem Cell changes her personality depending on where in the body she is located and the experiences she goes through. In a series of scenes, we see how Stine Stem Cell takes on new identities and abilities. Surrounded by fatty tissue, she becomes compliant and docile, she does not yearn to go anywhere. In contrast, living under the terror of a chronic inflammation, fat cells convince her to divide into many daughter cells. When the extremist CytoKen makes his entrance through YouTube, urging armed defense against an unknown enemy, immune cells turn against the body and allow a mature Stine mammary gland cell to evolve backwards into an immature stem cell again. At least that is who she believes she has become.

Stine with the identity of a mammary epithelial cell cannot resist some delicious estrogen offered by two friendly fat cells.

The play is interactive as the audience plays the role of Stine's surroundings. They receive costumes to allow identification with various characters: fat cells, fibroblasts, endothelial cells and immune cells who give instructions and perform actions which determine Stine's fate. There is a chance that a certain phagocyte lures the immune system into disarray, or that Stine's existence is made difficult by a traitorous fibroblast, stretching fibers across stage. Then it is good to know that everything can be reversed if only the surroundings behave properly. What happens to Stine Stem Cell in this chaos of war calls and dutiful milk production depends on the audience, and how they play their roles.

CytoKen is an anxious type urging the immune defense to wage war against a non-existent enemy.

The play is supported by CCBIO and the Vestland Fylkeskommune. In 2019, more than 800 schoolchildren in the Bergen area got to experience the tumor microenvironment on stage through 16 performances in schools and at the annual Research Fair. Henriette also collected data from visited schools, in order to document the effect of theatre used for public education. The feedback was very good.

Media Appearances

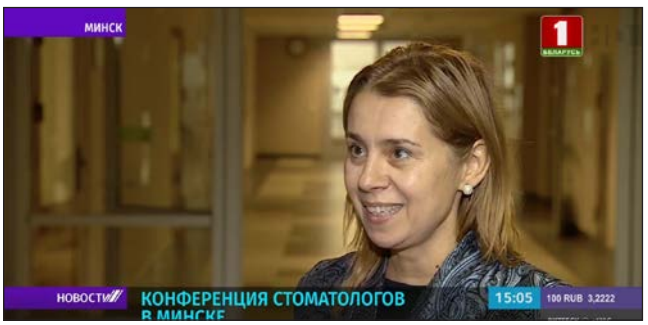
29.12.19 – BESTPRACTICE ONKOLOGI/HEMATOLOGI
"Et kjemoterapifritt behandlingsalternativ for pasienter med tilbakefall av eggstokkreft" – Line Bjørge

10.12.19 – DAGENS MEDISIN
"Slik kan kunstig intelligens endre bildemedisinen" – Ingfrid Haldorsen

05.12.19 – DAGENS MEDISIN
"En av to behandlinger handler om kreft" – Ole Frithjof Norheim

01.10.19 – DAGENS MEDISIN
"Milepæl for norsk kreftstudie" – Oddbjørn Straume

30.09.19 – TVR.BY – BELARUSSIAN NATIONAL TV
"Future dentists of Belarus, Norway, Moldova and Armenia to be trained in a joint program" – Daniela E. Costea



23.09.19 – NATIONEN
"Ny behandling mot arvelig eggstokkreft godkjent" – Line Bjørge

22.09.19 – BERGENS TIDENDE
"Dagen etter kreftoperasjonen kunne Tordis dra hjem. Da var hun ferdigbehandlet." – Camilla Krakstad, Ingfrid Haldorsen

22.09.19 – BERGENSAVISEN
"Forskning for liten og stor" – Henriette Ertsås

21.09.19 – BERGENSAVISEN PLUSS
"Her ble det forsket på stort og smått" – Henriette Ertsås

21.09.19 – TRØNDERAVISA
"Godkjenner ny behandling mot arvelig eggstokkreft" – Line Bjørge

20.09.19 – VG
"Ny behandling gir håp til pasienter med uhelbredelig eggstokkreft: – Største som har skjedd siden immunterapi" – Line Bjørge


VG

Ny behandling gir håp til pasienter med uhelbredelig eggstokkreft: – Største som har skjedd siden immunterapi

En ny behandling mot eggstokkreft har vist 70 prosent lavere risiko for tilbakefall eller død hos en testgruppe og er godkjent i Europa og USA. Torsdag ble behandlingen godkjent for alle pasienter i Norge i en begrenset periode.

20.09.19 – ABC NYHETER
"Ny behandling mot arvelig eggstokkreft godkjent i Norge" – Line Bjørge

20.09.19 – NORDVESTNYTT
"Ny behandling mot arveleg eggstokkreft godkjent i Noreg" – Line Bjørge

20.09.19 – DRAMMENS TIDENDE
"Ny kreftbehandling godkjent i Norge" – Line Bjørge

20.09.19 – FORSKNING.NO
"Ny behandling mot arvelig eggstokkreft godkjent i Norge" – Line Bjørge

20.09.19 – FJORDABLADET
"Ny behandling mot arveleg eggstokkreft godkjent i Noreg" – Line Bjørge

20.09.19 – MØRE
"Ny behandling mot arveleg eggstokkreft godkjent i Noreg" – Line Bjørge

20.09.19 – NORDRE
"Ny behandling mot arveleg eggstokkreft godkjent i Noreg" – Line Bjørge

19.09.19 – P4 RADIO
"Behandling mot eggstokkreft" – Line Bjørge

18.09.19 – KHRONO
"49 unge forskere konkurrerer om ti finaleplasser i Forsker Grand Prix" – Hilde Renate Engerud

06.09.19 – DAGENS MEDISIN
"Ta tak i genomforskningen!" – Inge Jonassen


DAGENS Medisin

Nyheter Debatt Pharma

DEBATT OG KRONIKK

Ta tak i genomforskningen!

Norge må bygge ut e-infrastrukturen for håndtering av genom-data.

Publisert: 2019-09-06 05.18
Finn Drabløs/Eivind Hovig/Inge Jonassen

Del:

04.09.19 – KHRONO
"Skal undersøke bruken av 6 milliarder forskningskroner" – CCBIO

15.07.19 – PÅ HØYDEN
"Musikk-medisineren" – Bjørn Tore Gjertsen


PÅ HØYDEN

Nyhetsavisen for Universitetet i Bergen

Musikk-medisineren

Bjørn Tore Gjertsen kom ikke til Bergen først og fremst for å studere medisin. Han kom for å spille i et av Norges beste brassband.

Hilde Kristin Strand

11.07.19 – HELSE BERGEN
"Gjennombruddsforskning fra KK om eggstokkreft" – Line Bjørge

10.07.19 – VG
"Ny forskning om eggstokkreft: – Et gjennombrudd" – Line Bjørge

27.06.19 – DAGENS MEDISIN
"Hva betyr bioteknologi for oss nå – og i fremtiden?"
– Ole Frithjof Norheim

DAGENS Medisin — Nyheter Debatt Pharma DM Arena

Hva betyr bioteknologi for oss nå – og i fremtiden?

Bør vi være fremtidsoptimister og omfavne all ny teknologi – eller være «føre-var» og innta en restriktiv holdning inntil vi vet nok om sikkerhet, nytte, personvern og utilsiktede etiske og samfunnsmessige konsekvenser?

Publisert: 2019-06-27 05.31
Ole Frithjof Norheim

Del:

Ole Frithjof Norheim

Etikk: ***Ole Frithjof Norheim****, professor i medisinsk etikk og samfunnsmedisin ved Universitetet i Bergen. Adjunkt professor ved Harvard T.H. Chan School of Public Health og ny leder av Bioteknologirådet*

FORSLAGET TIL endringer i bioteknologiloven er nå **sendt ut på høring** – med svarfrist til 2. september 2019.

Alle har mulighet til å bidra med sitt syn.

Utviklingen innen bioteknologi og samfunnet går fort – og

14.06.19 – ALLERS
"Senskader er svært vanlig" – Line Bjørge

Senskader er svært vanlig

Alle tre behandlingstypene ved kreft – kirurgi, strålebehandling og cellegift – kan gi bivirkninger og seneffekter. Dette gjelder ikke minst gynekologisk kreft.

Line Bjørge, seksjonsoverlege og professor ved Kvinneklinikken på Haukeland Universitetssjukehus, forteller at det er blir stadig mer fokus på seneffekter av kreftbehandling:
– Det er en pris å betale i forhold til alle tre behandlingstyper. Alle kan se friske ut etter behandling selv om de har betydelige plager, konstaterer hun.
Hvordan senskadene oppleves, varierer fra kvinne til kvinne og også hvor de er i livsforløpet. Det er for eksempel betydelig verre å få livmorhalskreft som ung, fordi en mister evnen til å få barn.

FÅR EN ANNEN KROPP
– Mange kvinner føler at de får en annen kropp. De føler at de mister seg selv. Og behandlingen fører til betydelig trøtthet. Jeg pleier å si at vi tar racergiret fra dem. Det handler ikke om vilje; det er rent fysisk.
Line Bjørge understreker at mange av pasientene som blir behandlet for gynekologisk kreft, lever mange år med god livskvalitet, selv om de kan ha mange plager. Hun peker på at kvinner har ulik mestringsevne og forskjellige strategier for å håndtere hverdagslivet. Noen har en veldig vanskelig sykdom, men lever likevel godt. Og omvendt.

BEST I VERDEN
Når det gjelder livmorhalskreft blir omtrent halvparten operert, mens resten behandles med stråling. De fleste tilfellene av livmorkreft blir operert, mens eggstokkreft blir behandlet med både kirurgi og cellegift.
– Norge er best i verden på behandling av livmorhalskreft. Utsiktene til å bli frisk igjen er veldig gode. Eggstokkreft har høyest dødelighet. 50 prosent blir ikke friske.

SCREENINGPROGRAM
Det viktigste alle kvinner kan gjøre er ifølge Bjørge å følge screeningprogrammene, altså møte opp til anbefalte undersøkelser, og å bli vaksinert.
– Og du skal aldri være redd for å gå til legen din med diffuse symptomer.
Line Bjørgen har jobbet med kreft i snart 30 år, og er optimist med tanke på fremtiden. Det skjer en utrolig rask utvikling innen kreftbehandling, med både økt kunnskap og økt tilgjengelighet av nye medikamenter.

EKSPERTEN: **Line Bjørge ved Haukeland Universitetssykehus.**

12 Allers 25/2019

14.06.19 – PR NEWSWIRE
"BerGenBio Presents Preliminary Phase II Clinical Data at EHA 24: Bemcentinib in Combination With Low Dose Chemotherapy Yields Durable Responses in AML Patients Unfit for Intensive Chemotherapy" – Bjørn Tore Gjertsen

14.06.19 – NETFONDS
"(BGBIO) BerGenBio presents preliminary Phase II clinical data at EHA 24: bemcentinib in combination with low dose chemotherapy yields durable responses in AML patients unfit for intensive chemotherapy" – Bjørn Tore Gjertsen

14.06.19 – OSLOBØRS
"BerGenBio presents preliminary Phase II clinical data at EHA 24: bemcentinib in combination with low dose chemotherapy yields durable responses in AML patients unfit for intensive chemotherapy" – Bjørn Tore Gjertsen

03.06.19 – DAGENS MEDISIN
"Eggstokk-kreft: – Vil ha stor betydning hvis man kan spare pasienten for cellegift" – Line Bjørge

29.05.19 – FARMATID.NO
"Farmaceutene gir 300 000 til forskning på kreft og hjerneslag" – Ragnhild Haugse

nft Farmatid.no — Norsk Farmaceutisk Tidsskrift

Ledige stillinger Aktuelt Vitenskap og fag Video Send inn manus Kontakt oss

Nyheter

Farmaceutene gir 300 000 til forskning på kreft og hjerneslag

Norges Farmaceutiske Forening deler ut to stipender på tilsammen 300 000 kroner til lovende forskning på kreft og hjerneslag.

Kommer godt med: *Ragnhild Haugse er strålende fornøyd med at Farmaceutene og leder Rønnaug Larsen gjør det mulig for henne å avslutte doktorgradsarbeidet sitt på en god måte.*

28.05.19 – BERGENS TIDENDE
"Bioteknologirådet flyttes til Bergen" – Ole Frithjof Norheim

28.05.19 – PÅ HØYDEN
"Verdensledende kreft-forsker besøkte UiB" (Valerie Weaver) – Donald Gullberg

Professor Valerie Weaver er verdensledende innenfor området mekanotransduksjon. Her snakker hun på konferanse i Bergen nylig.mm

Verdensledende kreft-forsker besøkte UiB

Den verdensledende kreftforskeren, Valerie Weaver, gjestet nylig Universitetet i Bergen på en internasjonal fibrosekonferanse.

22.05.19 – ALT OM DIN HELSE
"Var kreftsyk i syv år" – Oddbjørn Straume


HUDKREFTDAGEN

Var kreftsyk i syv år

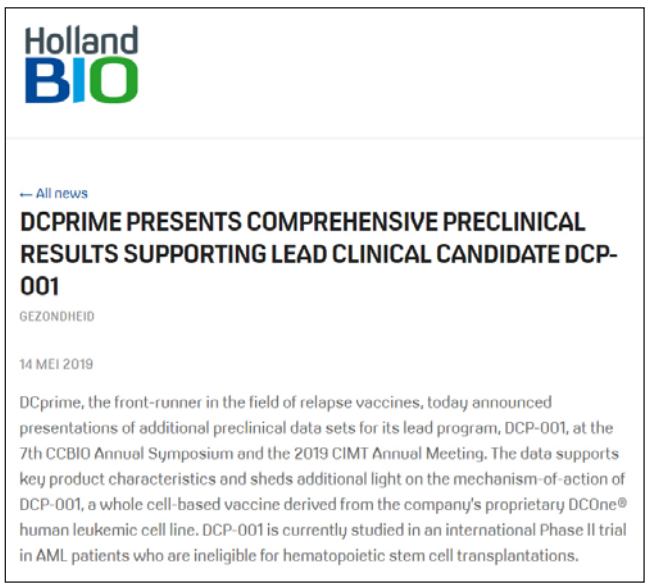
Tone Kvinnsland Amdal fikk fjernet en føflekk i 2009. Det viste seg at den var ondartet, og dette ble starten på en lang reise hvor kreften spredte seg til flere steder i kroppen.

Jeg hadde en føflekk i nakken som irriterte meg fordi den satt akkurat i genserkanten. Etter at

20.05.19 – TIDSSKRIFT FOR DEN NORSKE LEGEFORENING
"Confidential drug prices undermine trust in the system"
– Eirik Tranvåg

16.05.19 – FORSKERFORUM
"Forskningsrådet lagar plan for open forsking"
– Roger Strand

14.05.19 – HOLLANDBIO
"DCprime presents comprehensive preclinical results supporting lead clinical candidate DCP-001"
– 7th CCBIO Annual Symposium


Holland BIO

← All news

DCPRIME PRESENTS COMPREHENSIVE PRECLINICAL RESULTS SUPPORTING LEAD CLINICAL CANDIDATE DCP-001

GEZONDHEID

14 MEI 2019

DCprime, the front-runner in the field of relapse vaccines, today announced presentations of additional preclinical data sets for its lead program, DCP-001, at the 7th CCBIO Annual Symposium and the 2019 CIMT Annual Meeting. The data supports key product characteristics and sheds additional light on the mechanism-of-action of DCP-001, a whole cell-based vaccine derived from the company's proprietary DCOne® human leukemic cell line. DCP-001 is currently studied in an international Phase II trial in AML patients who are ineligible for hematopoietic stem cell transplantations.

14.05.19 – BIOSPACE
"DCprime Presents Comprehensive Preclinical Results Supporting Lead Clinical Candidate DCP-001"
– 7th CCBIO Annual Symposium

09.05.19 – FORSKNING.NO
"Fant ikke mer brystkreft med 3D-mammografi"
– Lars A. Akslen


forskning.no

Kultur Helse Miljø Samfunn Teknologi Naturvitenskap Blogg Forskersonen

Bildet viser radiologene Hildegunn Aase (bak) og Cecilia Sandvik ved Haukeland universitetssykehus i Bergen som tyder bilder fra 3D-mammografi. (Foto: Haukeland universitetssykehus).

Fant ikke mer brystkreft med 3D-mammografi

Fagmiljøer har hatt store forventninger til at den nye teknologien med mammografi i tre dimensjoner skal kunne avdekke enda flere aggressive og dødelige kreftsvulster i brystet. Men det slo ikke til, viser ny, norsk studie.

Anne Lisa Stranden
JOURNALIST

09.05.19 – HELSE BERGEN
"3D-mammografi: Mer treffsikkert – men fant ikke mer kreft" – Lars A. Akslen

08.05.19 – FORSKERFORUM
"Lagar plan for open forsking" – Roger Strand

22.04.19 – KHRONO
"162 nye navn som skal styre pengestrømmen til forskning"
– Inge Jonassen

15.04.19 – PÅ HØYDEN
"Disse skal sitte i Forskningsråds-styrer" – Inge Jonassen

24.04.19 – PÅ HØYDEN
"Christieprisen til Jan Einar Greve" – Lars A. Akslen


PÅ HØYDEN

Nyhetsavisen for Universitetet i Bergen

Christieprisen til Jan Einar Greve

12.04.19 – FORSKERFORUM
"Disse skal avgjøre om du får støtte fra Forskningsrådet"
– Inge Jonassen

10.04.19 – KHRONO
"Fra høgskole til universitet: Fare for kvasiakademisering av profesjoner" – Roger Strand

10.04.19 – NRK
"Ikke svekk Bioteknologirådet" – Ole Frithjof Norheim

04.04.19 – DAGENS MEDISIN
"Støttet Legemiddelverket i 31 av 34 saker"
– Eirik Joakim Tranvåg

01.04.19 – RANA BLAD
"Ranværing er ny leder for Bioteknologirådet"
– Ole Frithjof Norheim

29.03.19 – UROTODAY
"Elevated plasma interleukin 6 predicts poor response in patients treated with sunitinib for metastatic clear cell renal cell carcinoma" – Martin Pilskog, Oddbjørn Straume

April 2019 – GYNEKOLOGEN
"PARP-hemming i behandling av eggstokkreft"
– Liv Cecilie Vestrheim Thomsen, Line Bjørge

30.03.19 – VÅRT LAND
"Ny biotekleder" – Ole Frithjof Norheim

30.03.19 – BERGENSAVISEN
"Bergensprofessor overtar etter Kristin Halvorsen"
– Ole Frithjof Norheim

30.03.19 – DAGEN
"Han er ny leder for Bioteknologirådet"
– Ole Frithjof Norheim

29.03.19 – DAGENS MEDISIN
"Ole Frithjof Norheim blir leder av det nye bioteknologirådet" – Ole Frithjof Norheim

29.03.19 – BERGEN TIDENDE
"Norheim overtar som leder i Bioteknologirådet"
– Ole Frithjof Norheim

29.03.19 – DAGENS NÆRINGSLIV
"Ny leder for Bioteknologirådet" – Ole Frithjof Norheim

29.03.19 – BIOTEKNOLOGIRÅDET
"Ole Frithjof Norheim ny leder for Bioteknologirådet"
– Ole Frithjof Norheim

29.03.19 – DAGENS MEDISIN
"Hva er uetisk medisin?" – Ole Frithjof Norheim

21.03.19 – DAGENS MEDISIN
"Åpent? Nei! Rettferdig? Hvem vet?" – Eirik Joakim Tranvåg

21.03.19 – DAGENS MEDISIN
"Går hardt ut mot hemmelighold i helseprioriteringene"
– Ole Frithjof Norheim

21.03.19 – DAGENS MEDISIN
"Ledere må få opplæring i prioritering"
– Ole Frithjof Norheim

03.03.19 – BERGENS TIDENDE
"Denne fisken vil trolig få Parkinson" – Bjørn Tore Gjertsen

14.02.19 – BERGENS TIDENDE
"Forskere kurerte mus for diabetes"
– Heidrun Vethe

30.01.19 – MEDFAK
"Millioner til nytt senter for globale helseprioriteringer"
– Ole Frithjof Norheim

30.01.19 – FORSKNING.NO
"121 millioner til nytt senter for globale helseprioriteringer" – Ole Frithjof Norheim

13.01.19 – DAGENS MEDISIN
"Prioritering - en lederoppgave" – Ole Frithjof Norheim

Mini Biographies:
PhD Candidates and Postdocs 2019

ALAM, JAHEDUL
MS in biomedical sciences from Bonn, Germany, and was in 2019 a PhD candidate in the Gullberg group. His research project aimed to further characterize integrin α11 expression and function. He finished his PhD in January 2020, and title of his work was "Novel Insights into Integrin α11 Expression and Function."

ANANDAN, SHAMUNDEESWARI
MSc in biotechnology and is currently a PhD candidate in the groups of 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 exploration 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 and BRCA1 germline mutations.

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 on regulatory patterns in prostate cell differentiation, with investigation of the transcription factors AR, GATA2 and NKX3-1. Waqas is currently a postdoc in the Kalland group. His postdoc work aims for production of therapeutic monocyte-derived dendritic cells for new cancer immunotherapy.

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 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 a PhD candidate in the Krakstad group, and the 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.

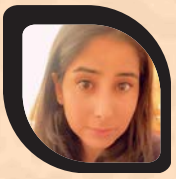
BERGSJØ, LOUISE EMBLEM
MS in chemistry from the University of Bergen and has since August 2017 been a PhD student in the Haug group, with McCormack and Ole Heine Kvernenes as co-supervisors. Her PhD project focuses on making peptides for PET, with an aim to develop a new method for radiolabeling of bioactive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

BISCHOF, KATHARINA
MD and consultant in obstetrics and gynecology, working at the Women´s Clinic, Haukeland University Hospital. She was a PhD candidate in the McCormack and Bjørge groups until her doctoral defense in February 2019 on p53 isoforms and preclinical imaging in high-grade serous carcinoma.

BJÅNES, TORMOD KARLSEN
MD and senior consultant in clinical pharmacology at Haukeland University Hospital. He is currently a PhD candidate in the McCormack group. His main focus is on the nucleoside analogue gemcitabine in pancreatic cancer, with emphasis on intracellular drug metabolite kinetics following sonoporation.

BØRRETZEN, ASTRID
MD from the University of Bergen. She is 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, pathologist, currently head of department and chief consultant at the Department of Pathology, Oslo University Hospital. She has since 2015 been a part-time PhD student in the Akslen group. Her PhD project focuses on breast cancer stroma and aims to identify the interplay between tumor-infiltrating lymphocytes, vascular invasion and stromal elastosis.



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

DAVIDSEN, KJERSTI TEFRE
MD from the UiB, and a PhD student in the Lorens and Straume groups until her doctoral defense in June 2019. Her PhD work focused on AXL mediated resistance to targeted therapy and immunotherapy, with an aim to increase the understanding of how 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 UiB. He is currently a PhD student in the Lorens group, with a project that aims to understand the immune interplay between 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 a PhD candidate at the University of Oslo, jointly with the Costea group. Her research project aims to identify prognostic biomarkers in oral cancer and premalignant disorders, particularly focusing on the prognostic role of the S100 A14 protein on progression and differentiation of oral squamous carcinoma.

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.

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 nano-diamonds.

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 ANDREA
MD from UiB, has been working as a resident in radiology in the Department of Radiology, Haukeland University Hospital. She is 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 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.

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 UiB, and a PhD student in the Gjertsen group until her doctoral defense in February 2020, working on precision haemato-oncology and FLT3 mutations in acute myeloid leukemia. The project aimed to elucidate aspects of clonal heterogeneity and evolution in acute myeloid leukemia, with specific focus on possible translational implications.

ENGERUD, HILDE RENATE
MD from UiB. She was a PhD candidate in the Krakstad group until her doctoral defense in February 2020, working on molecular markers to predict prognosis and guide therapy in endometrial cancer.

ESPEDAL, HEIDI
MS in medical cell biology and PhD in the field of neuro-oncology, both from UiB. Since late 2018 she has been a postdoc in the Krakstad group, with a focus on functional imaging of endometrial cancer mouse models.

FINNE, KENNETH
MS in molecular biology from UiB and finished in 2015 a PhD on proteomic changes in hypertensive kidney disease. He was a postdoc in the Akslen group until September 2019 and is now working as a senior engineer in the same group. His main areas of interest are tissue-based proteomics and imaging mass cytometry.

FONNES, TINA
VMD from The Norwegian University of Life Sciences and was until November 2018 a PhD candidate in the Krakstad group exploring cell lines, clinical samples and mouse models of endometrial cancer with special attention to imaging and therapeutic studies. Her PhD work focused on preclinical models and molecular biomarkers – tools to improve treatment in endometrial carcinoma. She is now a postdoc in the same group.

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.

GUERREIRO, EDUARDA
MSc in Biomedical Sciences from the University of Algarve, Portugal. She will complete her PhD studies in June 2020 at the Institute of Oral Biology, University of Oslo, connected to the Costea group. Her PhD project focuses on extracellular vesicles from oral cancer aiming at understanding their role in tumor progression.

GYARMATHY, GERGŐ
MS from the University of Szeged, Hungary. He is a PhD candidate in the Gullberg group. In his PhD work, Gergő is focusing on the molecular interactions of Integrin α11 with regards to Syndecan-4.

HAJJAR, EHSAN
MS in medical cell biology from the University of Bergen and has been a PhD candidate in the Gjertsen group since 2015. His project focuses on the modulation and function of p53 protein isoforms in acute myeloid leukemia. He is also examining the modulation of p53 protein isoforms in the leukemic cells treated by the AXL kinase inhibitor agent bemcentinib (BGB324).

HALLE, MARI KYLLESØ
MS in molecular biology from NULS and a PhD from UiB. She is currently a postdoc in the Krakstad 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 UiB in 2013. She is currently a postdoc in the Gjertsen group. Her research focuses on characterizing the effects of 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.

INGEBRIKTSEN, LISE MARTINE
MS in Biomedicine from the University of Tromsø - The Arctic University of Norway, and currently a PhD candidate in the Akslen group, with Elisabeth Wik as main supervisor. Her PhD project focuses on identifying clinically relevant biomarkers of aggressive breast cancer among the young, with potential for improving individualized treatment and outcome.

JACOB, HAVJIN
MS in molecular medicine from NTNU and a PhD from UiB 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. She is currently a postdoc in the Gjertsen group, focusing on biomarkers in clinical studies of advanced cancer. Of particular interest is liquid biopsies 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 UiB. 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.

KANG, JIYEON
PharmD, holds an MSc in global health from London School of Economics and Political science (LSE). She is a PhD candidate in the Health Economics group at the London School of Hygiene and Tropical Medicine (LSHTM), supervised by John Cairns, focusing on how real-world data could be utilized in Health Technologies Assessment (HTA) especially targeted cancer treatments.

KJØLLE, SILJE
MS in molecular biology from UiB, and currently a PhD candidate in the Akslen group. Her research project is focused on hypoxia patterns 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.

KLEFTOGIANNIS, DIMITRIOS
BC in computer science and engineering, MS in bioinformatics from the University of Patras, Greece and PhD in computer science in 2016 from King Abdullah University of Science and Technology (KAUST), focusing on computational identification of regulatory elements (enhancers and promoters) using genomic and epigenomic datasets. Currently he is a postdoc with the Computational Biology Unit (CBU) in the Jonassen group and also works towards the Akslen group. He is focusing on multi-omics datasets with machine learning to gain insights into cancer progression mechanisms.

KLEINMANNS, KATRIN
MS in Biomedicine from Hannover Medical School, Germany, and completed her PhD in the McCormack and Bjørge groups in December 2019. Her project focused on the development of immunocompetent patient-derived xenograft models of high-grade serous ovarian cancer. This aims to further improve therapeutic interventions by optimizing image-guided surgery and testing immunotherapies.

LEITCH, CALUM
MS in molecular and cellular biology from the University of Glasgow in 2012. Since 2012 he has been a PhD candidate in the Gjertsen group, focusing 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 UiB and until April 2019 a PhD candidate in the Lorens and Akslen groups. Her PhD project 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. She is now a postdoc in the Lorens group, working on imaging mass cytometry and high dimensional analysis of the tumor microenvironment.

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 of CCBIO, 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, NOËLLY
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 Technology in Sudan, and an MPhil in oral sciences from UiB. 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.

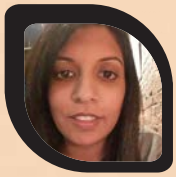
MOHAMED, NAZAR
Dentist, oral microbiologist and holds a BDS degree and MS in molecular medicine from the University of Khartoum, Sudan. He has since 2015 been a PhD student in the Costea group. His PhD project focuses on diversities of the salivary mycobiome and the patterns of volatile organic compounds 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
MSc in periodontics from the University of Khartoum. Since August 2016 she has been a PhD candidate in the Costea group. Her PhD project focuses on prognostic biomarkers in oral squamous cell carcinoma patients with specific focus on the inflammatory host reaction and its correlation to 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.

OMSLAND, MARIA
BSc in biomedical laboratory sciences and MSc and PhD in medical cell biology from 2017 from UiB. Omsland just returned from a 2-year long research stay as a visiting fellow at the National Institutes of Health (NIH) and is since august 2019 a postdoc in the Gjertsen group. In her postdoc project, she focuses on cell-to-cell communication and signaling in the bone marrow compartment of chronic myeloid leukemia before and during treatment with tyrosine kinase inhibitors. The main methods will be the new imaging mass cytometer (IMC) and 2-photon microscopy of living organisms.

PARAJULI, HIMALAYA
BS in dental surgery from the Tribhuvan University Nepal and did his PhD in 2016 on integrin α11 in oral carcinogenesis at UiB. He was a postdoc in the Costea group from 2017 to August 2019, doing research on melanoma brain metastasis. Currently he is a guest researcher in the Costea group.



PETERS, STACEY D'MELLO
PhD in molecular medicine from The University of Auckland. Currently a postdoc in the Lorens group. Her research focuses on tumor cell plasticity in malignant melanoma and its role in therapy resistance with a particular focus on AXL receptor kinase mechanisms.

PILSKOG, MARTIN
MD at the Department of Oncology, Haukeland University Hospital. He completed his PhD January 2020 in the Straume and Akslen groups. His thesis focused on the roles of interleukin 6 and interleukin 6 receptor as biomarkers of treatment response in relation to anti-angiogenesis treatment of metastatic renal cell carcinoma.

RAJTHALA, SAROJ
BS in biochemistry from Purbanchal University, Nepal and MS in medical cell biology from UiB. He has since 2015 been a PhD candidate in the Costea group. His research focuses on the identification of microRNA signatures in the tumor stroma that can be used as prognostic factors and for therapeutic intervention in oral squamous cell carcinoma.

SCHUSTER, CORNELIA
MD and 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.

SEFLAND, ØYSTEIN
MD from NTNU, the Norwegian University of Science and Technology, Trondheim. He initiated his PhD work in the Gjertsen group in the fall of 2019. His focus is on the use of dendritic cells as a therapeutic option in the treatment of the myeloid malignancies.

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 the London School of Hygiene and Tropical Medicine (LSHTM), and is currently a PhD candidate in the Health Economics group of CCBIO focusing on economic evaluations of cancer biomarkers under the supervision of Professor John Cairns at LSHTM. Kelly is completing her PhD work in spring 2020.

SHAFIEE, SAHBA
MS in biomedical cell biology from UiB, and a PhD student in the Gjertsen and McCormack groups until her doctoral defense in June 2019, working on translational development of preclinical models and therapies in myelodysplastic syndromes.

SLETTA, KRISTINE YTTERSIAN
BS in biomedical science, University of the Sunshine Coast, Australia and an MS in biomedicine, UiB. 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 UiB, currently a PhD candidate in the Akslen group (main supervisor Linda Stuhr). Her project is focused on the role of integrin α11β1 expression in breast cancer, in experimental models and in human breast cancer.

SULIMAN, SALWA
BDS from the University of Khartoum, Sudan, a PhD from UiB, 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.

SÆLE, ANNA KRISTINE MYRMEL
MD at the Department of Pathology, Haukeland University Hospital, and currently a PhD candidate in the Akslen group, with Elisabeth Wik as main supervisor. The project is focused on hormone receptor regulators and immune responses in primary and metastatic breast cancer.

THOMSEN, LIV CECILIE VESTRHEIM
MD, specialist in obstetrics and gynecology, and a PhD from UiB 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 for immune cells and checkpoint inhibitor responses in patient-derived materials. She also works on analyses of data from early phase clinical trials on prostate and ovarian cancer.

TISLEVOLL, BENEDICTE SJØ
MD from UiB and is currently a PhD candidate in the Gjertsen group. Her project is focused on early therapy response evaluation in acute myeloid leukemia, using Mass Cytometry (CyTOF) to investigate signaling events in immunophenotypical cell clusters to separate responders from non-responders.

TORKILDSEN, CECILIE FREDVIK
MD from UiB 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 UiB and currently a PhD candidate at the Bergen Centre for Ethics and Priority Setting (BCEPS) and part of CCBIO's 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.

VETHE, HEIDRUN
MS in medical cell biology and a PhD on stem cells research and diabetes, both from UiB. She is currently a postdoc in the Akslen group, focusing on identifying protein biomarkers and novel targets in aggressive breast cancer, with a special emphasis on the tumor microenvironment, using mass spectrometry-based proteomics, imaging mass cytometry and immunohistochemistry.

VIÑEGRA, ELVIRA GARCÍA DE JALÓN
BS in chemistry and a master in organic synthesis and medicinal chemistry from UiB. 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.

WAGNER-LARSEN, KARI STRØNO
MD from UiB, and a specialist in radiology. She is working on a PhD project in the Bergen Gynecologic Cancer Research Group, focusing on artificial intelligence guided imaging biomarkers in uterine cervical cancer. The project aims to identify novel imaging techniques that predict advanced tumor stages, metastases and reduced survival in patients with uterine cervical cancer.

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 UiB, and a PhD student in the Bergen Gynecologic Cancer Group until his doctoral defense in December 2019, on advanced imaging biomarkers in endometrial cancer and preoperative tumor texture analysis from MRI. The aim was to identify new imaging parameters for better preoperative risk-classification of endometrial carcinomas.

ÅSE, HILDEGUNN SIV
MD and radiologist who also holds an MS in health economics from UiB. Currently a PhD student in the Bergen Gynecologic Cancer Group. Her PhD project focuses on digital breast tomosynthesis (3D-mammography) in breast cancer screening, with data from the Tomosynthesis Trial in Bergen (the ToBe-trial), focusing on detection rates, reading times, doses, breast density and mammographic features, comparing results after screening with digital mammography (2D) versus digital breast tomosynthesis.

FACTS AND FIGURES 2019

PERFORMANCE INDICATORS

	2013	2014	2015	2016	2017	2018	2019	TOTAL
PUBLICATIONS	76	71	77	85	94	81	79	563
COMPLETED PHDS	5	6	3	10	12	9	8	53
EXTERNAL FUNDING MNOK	7.2	21.9	22.5	36.0	34.0	32.1	26.7	180
MEDIA APPEARANCES	39	11	32	31	54	40	68	275

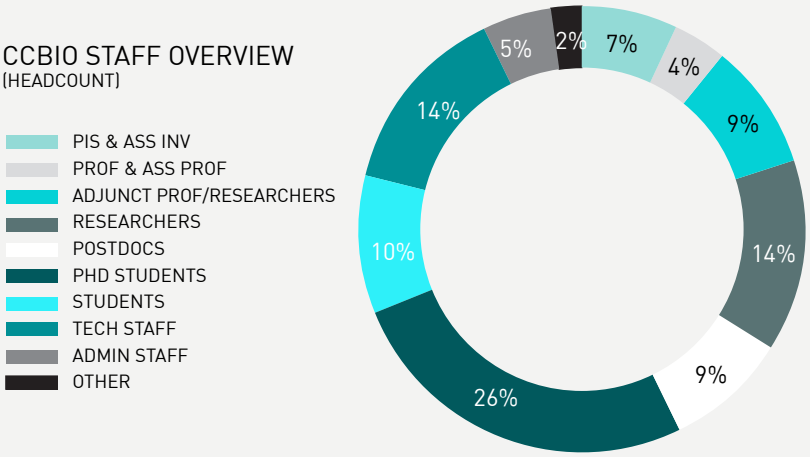
The table illustrates CCBIO's performance for 2013-2019. The scientific production is high. The reduction from 2017 is due to the first round of CoE financed PhDs and postdocs now having concluded their projects, publishing predominantly in 2016-2017. The influx of external funding is good, and numbers illustrate external funds consumed each year.

GENDER DISTRIBUTION
(HEADCOUNT)

TOTAL: 215 PERSONS

Of the 215 persons involved in the CCBIO enterprise, the gender distribution is female dominated with 66%. Among PhD students and postdocs, 67% and 75% are females respectively. This tendency shifts among professors and associate professors, where 38% are female. However, recruitment of excellent female staff to expand the CCBIO group of investigators has considerably lowered the male proportion in this group, with 27% 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)

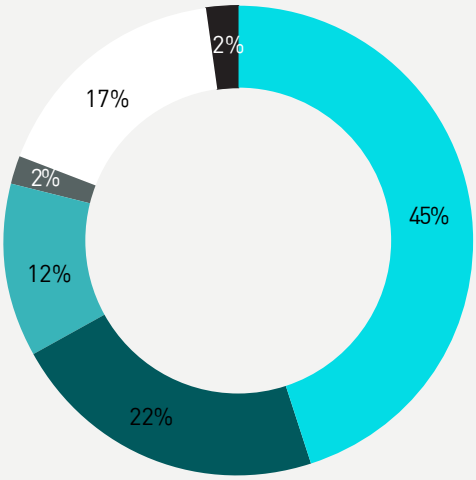


TOTAL: 215 PERSONS

CCBIO has a balanced composition of junior and senior researchers. The Centre is currently recruiting a number of postdocs and researchers, rather than PhDs, in order to increase the chances of major breakthrough findings. CCBIO has recruited younger investigators to full PI and associate PI status. These investigators are predominantly female, and further recruitment is expected to continue to 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 senior researchers, younger researchers and PhDs respectively. Three new members were recruited in 2019: Marta Bertolaso (Rome, Italy), Jonathan Irish (Nashville, USA) and Ursula Klingmüller (Heidelberg, Germany), bringing the total up to 16 adjunct positions for 2020.

FUNDING
(FUNDS USED IN 2019)

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

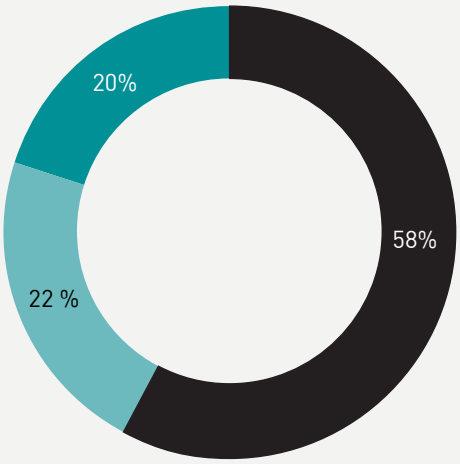


TOTAL = 77 MILL NOK

Total funds used in 2019 were 77 MNOK, of which 67% is the RCN CoE funding and own funding from UiB combined. The external funding consumed was 26.7 MNOK. This is 2 times the budgeted amount and illustrates a high success rate with public and especially private funding agencies. We expect to see an increase in external funds used as CCBIO makes increasingly more use of 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
- OTHER WESTERN COUNTRIES
- AFRICA & ASIA

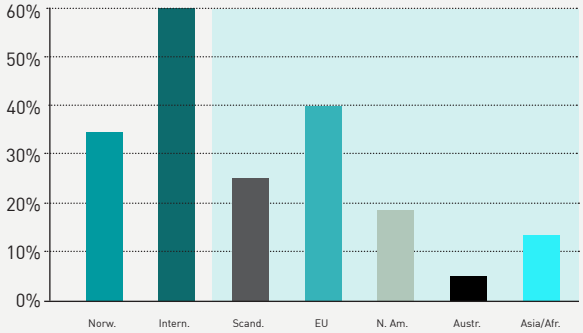


TOTAL: 215 PERSONS

CCBIO is an international CoE with 42% of its staff being of foreign nationalities. Among PhDs and postdocs, 49% and 40% originate from outside of Norway. Among CCBIO's senior researchers, 41% 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 58% of CCBIO's publications having at least one co-author from institutions abroad. International co-authorship has much stronger prevalence than collaborations with researchers from other Norwegian universities (34% of publications). Subdividing the international co-authorships into regions (grayed out color) demonstrates that CCBIO collaborates with institutions from most major regions worldwide. 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. For an overview of which countries and institutions CCBIO collaborates with, please see the network analyses on pages 138-139.

INTERNATIONALIZATION
(STAFF CO-AUTHORSHIP)

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



List of Personnel at CCBIO 2019

Name	Position	Academic title	Group
Aae, Liv Rebecca Arnedatter	Senior executive officer	MA	Administration
Akslen, Lars A.	Professor, Director of CCBIO	MD, PhD	Akslen
Aljiafiri, Asia	Master student		Costea
Amant, Frédéric	Adjunct professor	MD, PhD	CCBIO
Anandan, Shamundeeswari	PhD candidate	MS	McCormack/Bjørge
Andreassen, Kim	Advisor		Administration
Andresen, Vibeke	Senior researcher	MS, PhD	Gjertsen
Ardawatia, Vandana	Senior engineer	PhD	Akslen
Arnes, Jarle	Senior consultant	MD, PhD	Akslen
Askeland, Cecilie	PhD candidate	MD	Akslen
Aubert, Yves	Senior advisor	MSc, PhD	Administration
Augestad, Grete	Study nurse		Bjørge
Azeem, Waqas	Postdoc	MS, PhD	Kalland
Aziz, Sura Muhammed	Senior researcher	MD	Akslen
Bachmann, Ingeborg M.	Professor	MD, PhD	Akslen
Bakke, Ragnhild Maukon	Stud.Med. (Medical Student Research Programme)		Kalland
Benjaminsen, Susanne	Staff engineer	MSc	McCormack
Bentsen, Pål Tore	PhD candidate	MD	Gjertsen
Berg, Hege Fredriksen	PhD candidate	MS	Krakstad
Berge, Sissel Vik	Chief engineer		Lorens
Bergsjø, Louise Emblem	PhD candidate	MSc	McCormack
Beroukhim, Rameen	Adjunct researcher	MD, PhD	CCBIO
Bischof, Katharina	PhD candidate	MD, PhD	Bjørge
Bjørge, Line	Adjunct professor	MD, PhD, MBA	Bjørge
Bjånes, Tormod Karlsen	PhD candidate	MD	McCormack
Blanchard, Anne	Researcher	MA, PhD	Strand
Bougnaud, Sébastien	Researcher	MS, PhD	Lorens
Bourdon, Jean-Christophe	Adjunct researcher	MS, PhD	CCBIO
Bozickovic, Olivera	Staff engineer	MS, PhD	Krakstad
Branza, Dumitru	Guest researcher	MD	Costea
Bredin, Hanna	Stud.Med. (Medical Student Research Programme)		Krakstad

Name	Position	Academic title	Group
Brekken, Rolf	Adjunct professor	MD, PhD	CCBIO
Børretzen, Astrid	PhD candidate	MD	Akslen
Cairns, John	Adjunct professor	MA, MPhil	Cairns
Chen, Ying	PhD candidate	MD	Akslen
Chen, Ying Yi	Researcher		Lorens
Costea, Daniela Elena	Professor	DDS, PhD	Costea
Das, Ridhima	PhD candidate	DDS	Costea
Davidsen, Kjersti	PhD candidate	MD, PhD	Lorens/Straume
de Garibay, Gorka Ruiz	Postdoc	PhD	McCormack
de Montlaur, Constance de Villardi	Staff engineer	PhD	McCormack
Debnath, Kala Chand	Master student	DDS	Costea
Dhakal, Sushil	PhD candidate	MS	Lorens
Dhakal, Sushma Pandey	PhD candidate	DDS	Costea
Dillekås, Hanna	PhD candidate	MD	Straume
Dongre, Harsh	PhD candidate	MS	Costea/Bjørge
Dowling, Tara Helen	PhD candidate	MSc	Gjertsen/McCormack
Dybvik, Julie	PhD candidate	MD	Krakstad
Dyrkolbotn, Kjetil	Higher executive officer	MA	Administration
Edelmann, Reidun Jetne	Postdoc	MD, PhD	Akslen
Eide, Agnes Jørgensen	Stud.Med. (Medical Student Research Programme)		Krakstad
Eldevik, Kristine Fasmer	PhD candidate	MS	Krakstad
Enge, Elisabeth	Study nurse		Krakstad/Bjørge
Engelsen, Agnete	Researcher	MS, PhD	Lorens
Engen, Caroline Benedicte	PhD candidate	MSc, MD	Gjertsen/McCormack
Engerud, Hilde	PhD candidate	MD	Krakstad
Eriksen, May Gjerstad	Staff engineer	MSc	McCormack
Espedal, Heidi	Postdoc	MS, PhD	Krakstad
Fagerholt, Oda Helen Eck	Stud.Med. (Medical Student Research Programme)		Gjertsen
Fandalyuk, Zinayida	Staff engineer	MS	McCormack
Finne, Kenneth	Postdoc/senior engineer	MS, PhD	Akslen
Fonnes, Tina	Postdoc	DVM, PhD	Krakstad
Forsse, David	PhD candidate	MD	Krakstad
Forthun, Rakel Brendsdal	Researcher	MS, PhD	Gjertsen
Fosse, Vibeke	Researcher, veterinarian	DVM	McCormack/Bjørge
Fromreide, Siren	Chief engineer	MSc	Costea
Gabra, Hani	Adjunct professor	MD, PhD	CCBIO
Gabrielsen, Tommy Staahl	Professor	MA, PhD	Cairns
Garujel, Rashmi Chetri	Master student	DDS	Costea
Gavasso, Sonia	Researcher	MS, PhD	Gjertsen
Gelebart, Pascal	Researcher	PhD	McCormack
Gjertsen, Bjørn Tore	Professor	MD, PhD	Gjertsen
Golburean, Olga	Master student		Costea
Grøndal, Sturla Magnus	Researcher	MS	Lorens
Grønning, Mona	Chief engineer		Gullberg
Guerreiro, Eduarda	PhD candidate	MS	Costea
Gullaksen, Stein Erik	Researcher	MS, PhD	Gjertsen
Gullberg, Donald	Professor	MS, PhD	Gullberg
Gyarmathy, Gergő	PhD candidate	MS	Gullberg
Hagen, Maria Helene	Dental student (Medical Student Research Programme)		Costea
Hajjar, Ehsan	PhD candidate	MS	Gjertsen
Haldorsen, Ingfrid Salvesen	Adjunct professor	MD, PhD	Krakstad
Halle, Mari Kyllesø	Postdoc	MS, PhD	Krakstad
Hallseth, Gerd Lillian	Chief engineer		Akslen
Halvorsen, Ole Johan	Professor	MD, PhD	Akslen
Harkestad, Kjetil	Senior executive officer	MA	Administration
Haugse, Ragnhild	PhD candidate	MSc	McCormack
Heljasvaara, Ritva	Adjunct researcher	MS, PhD	CCBIO
Hellesøy, Monica	Postdoc	MS, PhD	Gjertsen
Hjelle, Sigrun Margrethe	Senior administrative officer	MS, PhD	Gjertsen
Hjelmeland, Marta Espevold	Master student		Krakstad
Hoang, Hua My	Staff engineer		Kalland
Hove, Elisabeth	Senior executive officer		Administration
Hovland, Randi	Senior researcher	MS, PhD	Gjertsen

List of Personnel at CCBIO 2019

Name	Position	Academic title	Group
Hua, Yaping	PhD candidate	MS	Kalland
Hugaas, Ulrikke	Stud.Med. (Medical Student Research Programme)		Akslen/Wik
Hugdahl, Emilia	Researcher	MD, PhD	Akslen
Høgås, Mildrid Bønes	Senior executive officer		Administration
Høivik, Erling André	Researcher	MS, PhD	Krakstad
Høysæter, Trude	Staff engineer		Gjertsen
Ingebriktsen, Lise Martine	PhD candidate	MSc	Wik/Akslen
Jacob, Havjin	Postdoc	MS, PhD	Krakstad
Jacobsen, Martha Rolland	Dental student (Medical Student Research Programme)		Costea
Jahedul, Alam	PhD candidate	MS	Gullberg
Jebsen, Nina Louise	Postdoc	MD, PhD	Gjertsen
Johannessen, Anne Christine	Professor	MD, DDS, PhD	Costea
Jonassen, Inge	Professor	MS, PhD	Jonassen
Kalland, Karl-Henning	Professor	MD, PhD	Kalland
Kalvenes, May Britt	Senior engineer	MS, PhD	Akslen/Costea
Kang, Jing	PhD candidate	MD	Lorens
Kang, Jiyeon	PhD candidate	MSc	Cairns
Kjølle, Silje	PhD candidate	MS	Akslen
Kleftogiannis, Dimitrios	Postdoc	PhD	Jonassen/Akslen
Kleinmanns, Katrin	PhD candidate	MS, PhD	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	MS, PhD	Krakstad
Kusche-Gullberg, Marion	Professor	MS, PhD	Gullberg
LaBarge, Mark	Adjunct professor	MS, PhD	CCBIO
Ladstein, Rita Grude	Adjunct associate professor	MD, PhD	Akslen
Langer, Anika	Researcher	PhD	McCormack
Leitch, Calum	PhD candidate/researcher	MS	Gjertsen/McCormack
Liang, Xiao	Researcher	DDS, PhD	Costea
Lindholm, Stein Rune	Research technician		Technical support
Litlekalsøy, Jorunn	Guest researcher	MS, PhD	Costea
Lorens, James B.	Professor	MS, PhD	Lorens
Lotsberg, Maria Lie	Postdoc	MS, PhD	Lorens
Lu, Ning	Senior engineer	MS, PhD	Lorens/Gullberg
Luís, Ana Beatriz Mateus D'Avó	PhD candidate	MA	Cairns
Lura, Njål Gjerde	PhD candidate	MD	Krakstad
Løken, Geir Olav	Administrative leader	MA	Administration
Madeleine, Nöelle	Postdoc	PhD	Lorens
Madissoo, Kadri	Senior engineer	MS	Krakstad
Manrikyan, Gayane	Guest researcher	DDS	Costea
McCormack, Emmet	Professor	MS, PhD	McCormack
Mills, Ian	Adjunct professor	PhD	CCBIO
Mohamed, Hassan Abdel Raof-Ali	PhD candidate	DDS	Costea
Mohamed, Nuha Gafaar	PhD candidate	DDS	Costea
Motzfeldt, Inga Kirstine Flaaten	Staff engineer	MS	Gjertsen
Musiime, Moses	PhD candidate	MS	Gullberg
Myrvold, Madeleine	Stud.Med. (Medical Student Research Programme)		Krakstad
Nazar, Mohamed	PhD candidate	DDS	Costea
Neppelberg, Evelyn	Adjunct associate professor	DDS, PhD	Costea
Nginamau, Elisabeth Sivy	Researcher	MD, PhD	Costea
Nguyen, Rebecca	Lab technician		Gjertsen
Nilsen, Irmelin Wilhelmsen	Guest researcher	M.Phil.	Strand
Norheim, Ole Frithjof	Professor	MD, PhD	Norheim
Omsland, Maria	Postdoc	MS, PhD	Gjertsen
Pantel, Klaus	Adjunct professor	MD, PhD	CCBIO
Papian, Andrew	Guest researcher	MD	Costea
Parajuli, Himalaya	Postdoc	DDS, PhD	Costea
Peters, Stacey Ann D'Mello	Postdoc	PhD	Lorens
Pilskog, Martin	PhD candidate	MD	Straume/Akslen
Popa, Mihaela Lucia	Staff engineer, veterinarian	DVM	McCormack

Name	Position	Academic title	Group
Pridesis, Ann-Helen	Study nurse		Krakstad
Rajthala, Saroj	PhD candidate	MS	Costea
Ramnefjell, Maria	Researcher	MD, PhD	Akslen
Rane, Lalit Shirish	Researcher	MS, PhD	Gjertsen
Rayford, Austin	Master student		Lorens
Reed, Rolf K.	Professor	MD, PhD	Reed
Riise, Julie	Associate professor	MA, PhD	Cairns
Rozmus, Ezekiel Richard	Staff engineer	MSc	McCormack
Sabir, Misbah	Staff engineer	MSc	Gjertsen
Safont, Mireia Mayoral	Staff engineer		McCormack
Salvesen, Gerd Signe	Staff engineer		Reed
Schuster, Cornelia	Postdoc	MD, PhD	Straume/Akslen
Sefland, Øystein	PhD candidate	MD	Gjertsen
Seo, Mikyung Kelly	PhD candidate	MA	Cairns
Shafiee, Sahba	PhD candidate	MS, PhD	Gjertsen/McCormack
Siraji, Muntequa Ishtiaq	Staff engineer		Lorens
Siyam, Diana	Dental student (Medical Student Research Programme)		Costea
Sletta, Kristine Yttersian	PhD candidate	MS	Gjertsen
Smeland, Hilde Ytre-Hauge	PhD candidate	MD	Akslen/Reed
Solheim, Marion	Advisor		Administration
Stefansson, Ingunn	Professor	MD, PhD	Akslen
Stenmarck, Mille Sofie	Guest researcher	MD	Strand
Stigen, Endre	Staff engineer	MSc	Lorens
Strand, Elin	Researcher		Krakstad
Strand, Roger	Professor	Dr.Scient.	Strand
Straume, Oddbjørn	Professor	MD, PhD	Straume
Stuhr, Linda	Professor	MS, PhD	Reed
Suliman, Salwa	Postdoc	DDS, PhD	Costea
Svanøe, Amalie	Stud.Med. (Medical Student Research Programme)		Wik/Akslen
Sværi, Bård Kjetil Bratli	Leading research technician		Technical support
Sæle, Anna Kristine Myrmel	PhD candidate	MD	Wik/Akslen
Sødal, Marte	Master student		Krakstad
Sørlie, Therese	Adjunct professor	MD, PhD	CCBIO
Tegnander, Amalie Fagerli	Stud.Med. (Medical Student Research Programme)		Wik/Akslen
Thakur, Dinbandhu	Master student		Costea
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	PhD candidate	MD	Gjertsen
Torkildsen, Cecilie Fredvik	PhD candidate	MD	Bjørge
Tranvåg, Eirik Joakim	PhD candidate	MD	Norheim
Trovik, Jone	Professor	MD, PhD	Krakstad
Tveiterås, Maria	Staff engineer		Reed
Vethe, Heidrun	Postdoc	PhD	Akslen
Vidhammer, Eli Synnøve	Senior executive officer		Administration
Viñegra, Elvira García de Jalón	PhD candidate	MSc	McCormack
Wagner-Larsen, Kari Strøno	PhD candidate	MD	Krakstad
Wangen, Rebecca	Chief engineer	MS	Gjertsen
Watnick, Randolph	Adjunct researcher	MD, PhD	CCBIO
Wik, Elisabeth	Associate professor	MD, PhD	Akslen/Wik
Wimalarasan, Akilina	Master student		Jonassen
Winge, Ingeborg	Senior engineer	PhD	Akslen
Xenaki, Victoria	PhD candidate	DDS	Costea
Ytre-Hauge, Sigmund	PhD candidate	MD, PhD	Krakstad
Zaraq, Tariq Jan	Master student		Costea
Zhuoyan, Zhang	Guest researcher	DDS	Costea
Östman, Arne	Adjunct professor	MD, PhD	CCBIO
Øyan, Anne Margrethe	Senior researcher	MS, PhD	Kalland
Åse, Hildegunn Siv	PhD candidate	MD	Krakstad

List of publications 2019

CCBIO - List of Publications 2019

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

Bjånes TK, Jordheim LP, Schjøtt J, Kamceva T, Cros-Perrial E, Langer A, Ruiz de Garibay G, Kotopoulis S, McCormack E, Riedel B. Intracellular Cytidine Deaminase Regulates Gemcitabine Metabolism in Pancreatic Cancer Cell Lines. *Drug Metab Dispos*. 2020 Mar;48(3):153-158. doi: 10.1124/dmd.119.089334. Epub 2019 Dec 23.

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Lende TH, Austdal M, Varhaugvik AE, Skaland I, Gudlaugsson E, Kvaløy JT, Akslen LA, Søiland H, Janssen EAM, Baak JPA. Influence of pre-operative oral carbohydrate loading vs. standard fasting on tumor proliferation and clinical outcome in breast cancer patients — a randomized trial. *BMC Cancer*. 2019 Nov 8;19(1):1076. doi: 10.1186/s12885-019-6275-z.

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Grønningsæter IS, Fredly HK, Gjertsen BT, Hatfield KJ, Bruserud Ø. Systemic Metabolomic Profiling of Acute Myeloid Leukemia Patients before and During Disease-Stabilizing Treatment Based on All-Trans Retinoic Acid, Valproic Acid, and Low-Dose Chemotherapy. *Cells*. 2019 Oct 10;8(10). pii: E1229. doi: 10.3390/cells8101229.

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Tsuruda KM, Bhargava S, Akslen LA, Bjørndal H, Hofvind S. Pathway times in the mammography programme before and after introduction of the breast cancer care pathway. *Tidsskr Nor Laegeforen.* 2019 Sep 9;139(12). doi: 10.4045/tidsskr.18.0322. Print 2019 Sep 10. Norwegian.

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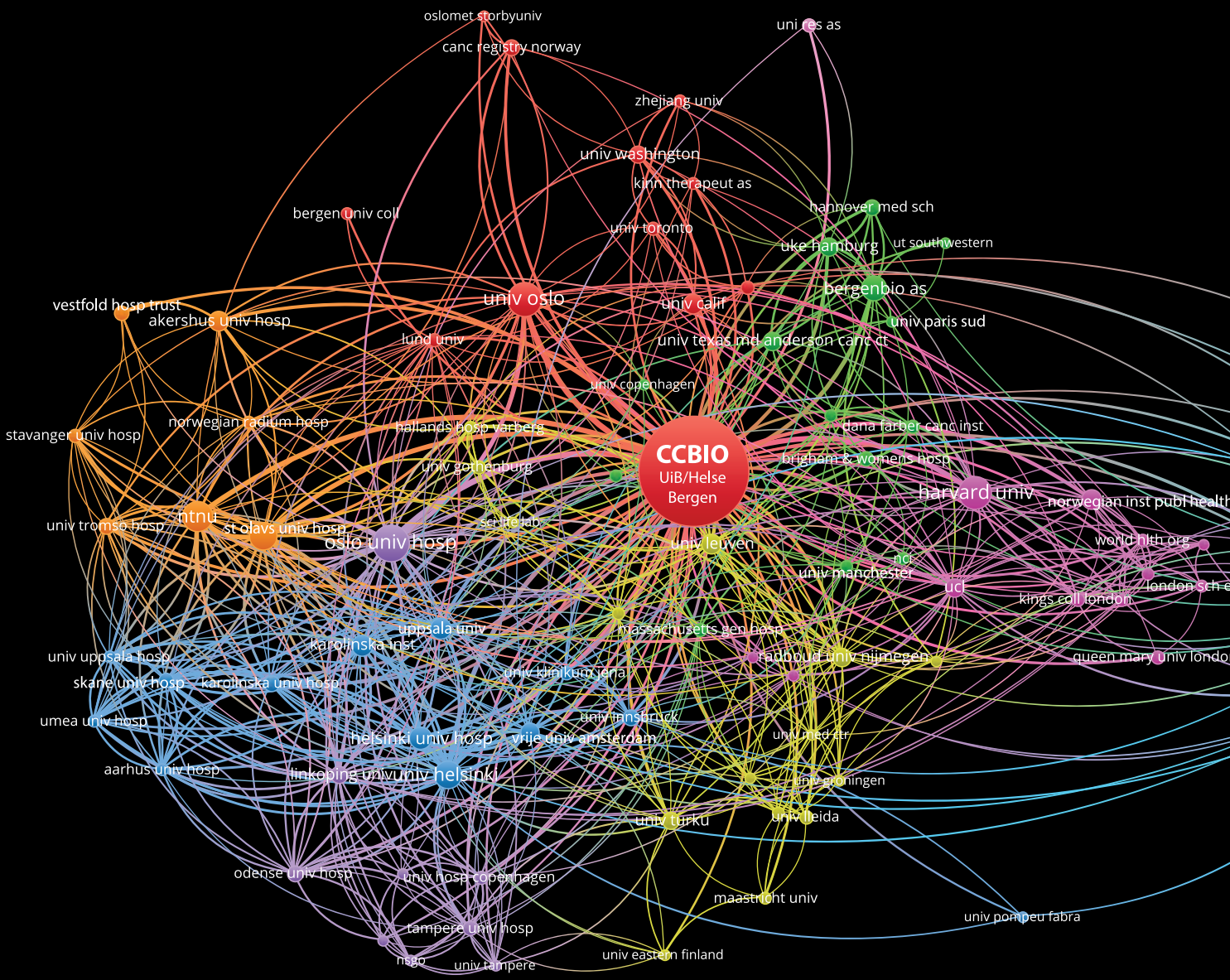
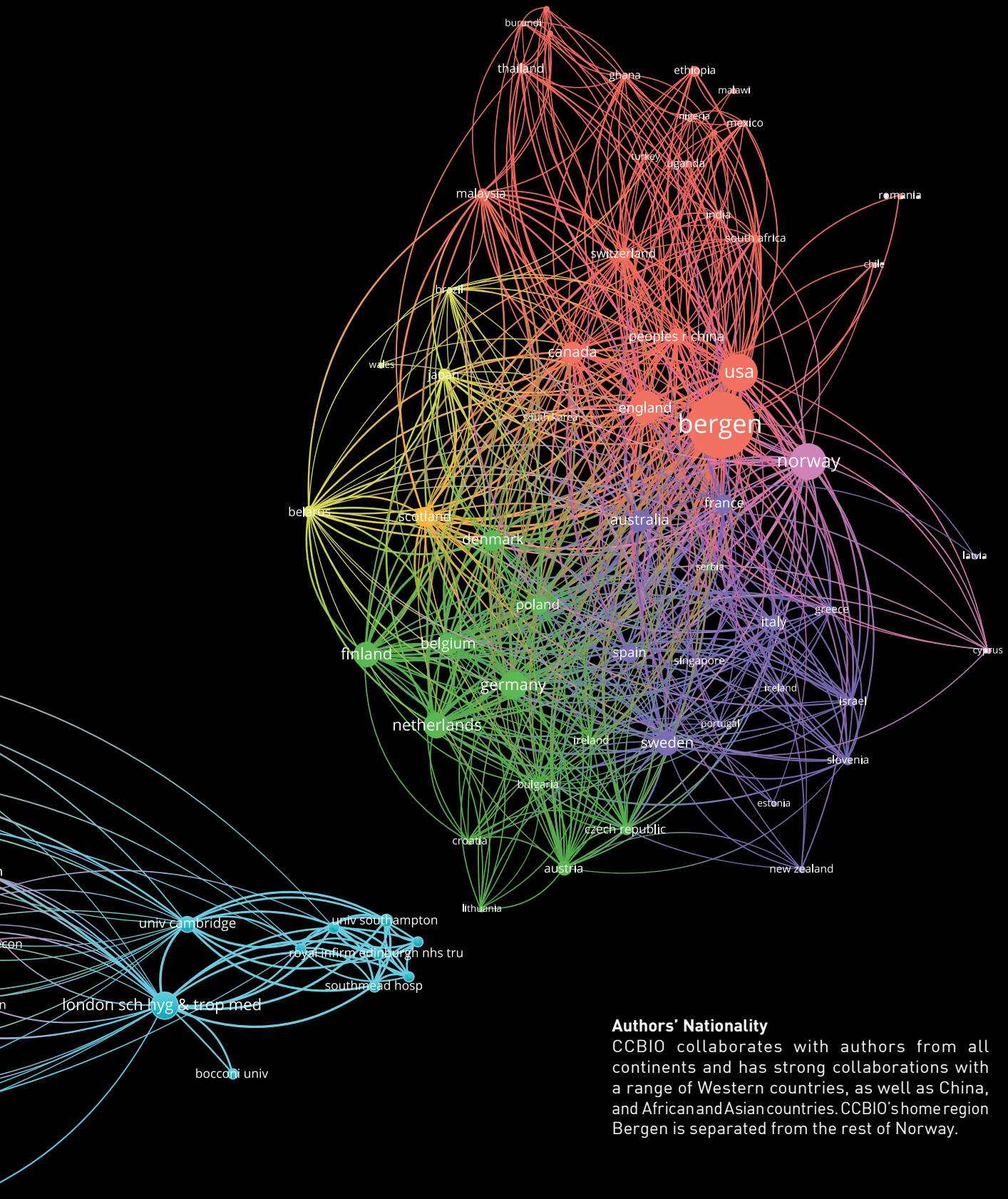
CCBIO's Collaborative Cosmos

The figures reflect bibliometric analyses of the nationality and institutional affiliation of authors on CCBIO's publications during the period 2013-2019. The thickness of the lines illustrates the strength of relations between authors, and the size of the dots illustrate the amount of authorships. The distance between various circles gives a rough illustration of the relative frequency of co-authorships between these nationalities and institutions.

Authors' Institutional Affiliation

CCBIO collaborates with authors from multiple internationally leading institutions, in addition to a range of Norwegian institutions. Internationally, relations with European and US institutions are especially prominent.





Authors' Nationality

CCBIO collaborates with authors from all continents and has strong collaborations with a range of Western countries, as well as China, and African and Asian countries. CCBIO's home region Bergen is separated from the rest of Norway.

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