Centre for Cancer Biomarkers

Norwegian Centre of Excellence – University of Bergen

Norwegian Centre of Excellence

The Research Council of Norway

ANNUAL REPORT 2020

Highlights

- **22 //** Scientific Activities and Progress
- **31 //** Research Teams
- **72 //** International Faculty
- **80 //** Research School
- **94 //** CCBIO Masterclass Program
- **114 //** Media Apparances
- **141 //** Publications

Contents

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Director's comments

During 2020, we all went viral and virtual. The COVID-19 pandemic became an unexpected and unprecedented challenge, and CCBIO-20 has done its best to step up and rewire a range of activities. Paradoxically, this adaptation process has presented possibilities for improvements. We have followed a very steep learning curve, both in science and society, and at many different levels. Regarding the disease itself, the need for precise biomarkers to predict aggressive conditions certainly represent a parallel to some of our challenges in the cancer field. Cost-calculations are important, and currently, compliance with guidelines is a major issue.

Our responses to the pandemic demonstrate how we can do things differently. Many of our seminars, courses and other events have become web-based, with increased attendance rates and significant international participation. *In situ* meetings have been replaced by *in zoom* interaction, and the emerging zoom fatigue has been realized. Notably, the stimulating small-talk has been difficult and limited, and "social closeness" has been reduced to a minimum.

With reduced activities in our laboratories during 2020, CCBIO has still had an active year. Among the most immediate consequences, our main gathering at Solstrand, the CCBIO Annual Symposium, had to be cancelled, and this educational and joyous networking event has been sorely missed by all of us. In the chapter on Scientific activities and progress, some of our reported results have been briefly described, on various biomarkers and how these can be applied in clinical settings. Our efforts in the field of multi-marker profiling of single cells and cell-signaling, in liquid or solid states, have continued by using our mass cytometry platform.

We are proud that two of our candidates finished their thesis work on health economics during late 2020, the first ever for CCBIO in this field. Dr. Kelly Mikyung Seo was awarded her PhD by the London School of Hygiene and Tropical Medicine for her thesis titled "Economic evaluations of companion cancer biomarkers for targeted therapies". The thesis by Dr. Ana Beatriz Luís titled "Essays on Economic Incentives and Implications of Biomarker Tests" was accepted for defense at UIB in 2020 and successfully defended in early 2021.

Four CCBIO Opinion pieces are included in this Annual Report. Engelsen and coauthors describe the many complex challenges in todays' precision medicine field. Despite the powerful methods of mutational profiling, only limited success can be seen in terms of treatment efficacy. The need for more functional phenotypic biomarkers and adaptive therapy is evident. Tranvåg discusses how cancer drugs are funded and prioritized. More and more costly treatments, with modest and uncertain benefits, are appraised by the drug reimbursement system, and the author argues that the system for evaluating cancer therapies has to change, for example by establishing guidelines and frameworks for socially responsible licensing, and by drug repurposing to reduce costs. In an interesting piece on breast cancer prevention, LaBarge argues that microenvironment-based drivers at the epi-genetic level are important to understand breast cancer incidence, and he discusses how the disease can possibly be prevented. A deeper understanding of the biology of aging is essential to increase our knowledge in this field. Finally, Cleuren presents some reflections on career development for young talents. How is it possible to better bridge the gap between the recruitment level and faculty positions? What are the available tools? A career plan is essential, as is active and organized CV-building and careful mentoring. For these reasons, the CCBIO Masterclass Program was launched during 2020 to promote career development.

What have we all learned this last year? The importance of adaptation and flexibility, continuous learning, and how to meet unexpected challenges, are really some of the key hallmarks of progress, for science and for the society. As these few lines are written, we face another COVID-19 wave in our country, and the problems are not over. As in science, it is important to be both realistic and optimistic, and to keep up the good work.

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 precise, 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 tumor microenvironment niches reflects cancer complexity and heterogeneity and determine cancer prognosis, beyond what is given by profiling of genetic alterations in tumor cells.

CCBIO concentrates on the following overlapping and integrated programs:

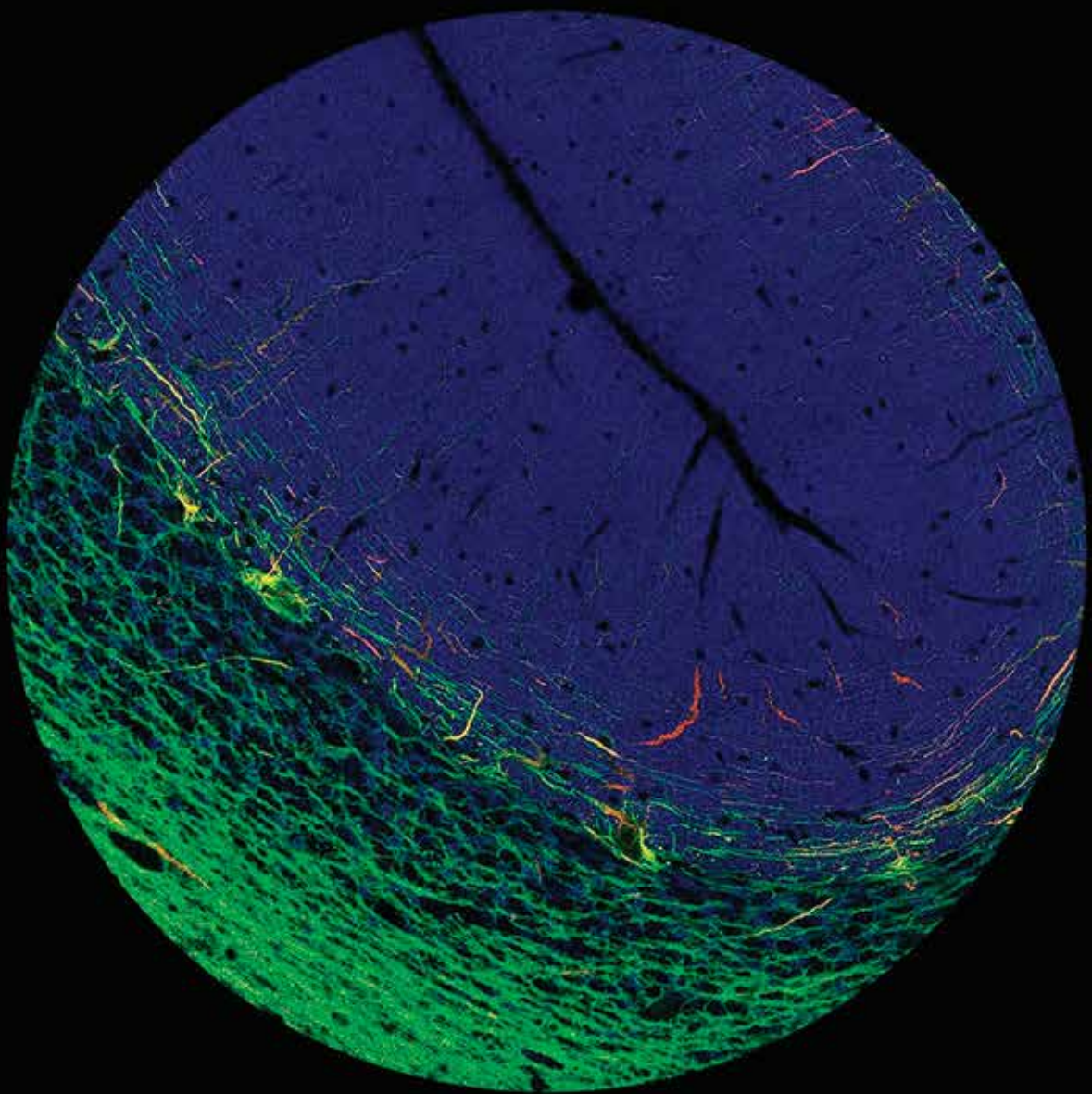
1. Mechanisms of Tumor-Microenvironment Interactions (Basic Studies)

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 by integrated ethics and economics projects, focused on how to fund and prioritize expensive cancer treatment in the era of expanding and costly personalized medicine. Collaboration partners, both national and international, have been recruited to support these programs.



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 and equipment, are located at the Faculty of Medicine's Departments of Clinical Medicine, Clinical Science, and Biomedicine. CCBIO also has activity and staff at the Centre for the Study of the Sciences and the Humanities, the Departments of Global Public Health and Primary Care, Economics, and Informatics, as well as at the London School of Hygiene and Tropical Medicine. Haukeland University Hospital is an important partner with contributions towards CCBIO both in terms of staff, facilities, such as the Clinical Trials Unit, and collaboration on advanced equipment, e.g. the Hyperion Imaging System.

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 the increasing collaboration within CCBIO. In 2020, most meetings were held online (after March 12).

Management group
In 2020, CCBIO was managed by the director, Lars A. Akslen, the co-director, Bjørn Tore Gjertsen, and the administrative leader, Geir Olav Løken. The management is advised by a research advisor and a strategic advisor, and also assisted by the web- and newsletter editor, an economy coordinator, a PhD coordinator, a number of finance officers, the faculty communications officers and a range of other administrative staff allocated to CCBIO in parts of their positions. CCBIO's head office (the "CCBIO-HQ") is located at the second floor of the Haukeland University Hospital's main building.

Integration with the host institution and administrative support
In terms of administrative support, CCBIO aims to use its funds as efficiently as possible towards its research aims, while also ensuring excellent administrative services for its researchers 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 and administrative support units.

As a main principle, funds and positions are located at the respective department where the research and teaching activities take place. This enables researchers to interact with their familiar support staff, thereby minimizing resources used on day-to-day administration. In addition, it reduces CCBIO's vulnerability and creates common interests between CCBIO and its departments. This model has proven successful due to its efficiency and robustness and has ensured excellent collaborative relations. ••

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

CCBIO Opinion

Text: Agnete ST Engelsen, Bjørn Tore Gjertsen, James Lorens, CCBIO

Challenges in contemporary precision medicine

According to the NIH, precision medicine is "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person" (NIH Precision Medicine Initiative). Targeted cancer therapy has been the poster child for precision medicine. In this regard, the NCI Molecular Analysis for Therapy Choice (NCI-MATCH) clinical trial, the largest precision oncology trial to date with over 6000 patients enrolled, is a milestone[1]. NCI-MATCH demonstrated the utility of next-generation sequencing in clinical practice, showing that 38% of cancer patients have currently "actionable" mutations. However, the results of the trial also highlight the challenges: only a minority of patients experienced clinical benefit, and many tumors were resistant to targeted inhibition. Hence, there remains a need to understand how tumors acquire therapy resistance. This will likely involve novel combination treatments; indeed, a follow-up clinical study, NCI-ComboMATCH, will test drug combinations to increase responses.

An interesting observation from the NIH-MATCH trial was that in comparison with TCGA data, standard cancer treatments did not lead to a substantial increase in gene mutations, emphasizing the role of non-genetic mechanisms of acquired resistance. However, tumor clonal selection of cognate mutations that render targeted therapies ineffective (e.g. EGFR T790M) were highlighted by the investigators. Other likely mechanisms of resistance include modulation of molecular pathways within the cancer cells, including pathway reactivation, bypass and indifference[2].

Given the astonishing genetic and non-genetic heterogeneity of cancers, how do we move forward? Ideally, identification of genetic and non-genetic drivers of acquired therapeutic resistance will enable the development of novel combination treatment strategies that prevent the evolution of drug resistance. This is facilitated by advances in single-cell technologies such as single-cell RNA sequencing and imaging mass cytometry (IMC) that allow deep phenotypic characterization of tumors. The growing use of these techniques to analyze longitudinal on-treatment biopsy samples in concert with ever more sophisticated computational analysis is creating a new level in our understanding of the dynamic tumor immune microenvironment. A major challenge will be to develop robust next-generation predictive companion biomarkers incorporating this information for clinical application. It should be noted that a comprehensive epidemiological study of adverse effects associated with additional on-treatment biopsies is lacking, highlighting the necessity for innovative patient-derived organoid technologies to supplement longitudinal biopsy sampling[3-4].

In January 2021, the Norwegian Ministry of Health and Care Services provided a national action plan for clinical trials 2021-2025[5]. The main goals are that the number of clinical trials should double and that 5% of patients in the specialist health service are enrolled in clinical trials by 2025. This includes a focus to equip Norway for personalized medicine. Thus, IMPRESS-Norway is a nation-wide cancer study initiated in 2021 as a public-private partnership where industry partners provide medications approved by the Norwegian Medicines Agency for use outside standard indications. The aim is to allocate patients to approved medications based on the molecular profiles of their cancers. This includes establishment of a national genome-center with expertise in medicine, genetics, pathology, bioinformatics and ICT security, integrating therapy guidance through a virtual molecular tumor board[6]. This integration of diverse disciplines has been a major obstacle, and thus represents an important step towards the realization of precision medicine in Norway.

The IMPRESS-Norway study, based on the Dutch DRUP-initiative[7], seeks to harmonize with similar studies in the Nordic countries. These large projects build on the principles and lessons from NCI-MATCH and similar trials; IMPRESS-Norway includes a strategy to build scientific rationale for novel phase II-III trials with a focus on rare cancers where alternative paths to conditional market approval are needed.

Potentially, this initiative can serve as a platform for future biomarker-based clinical trials. It is possible that the optimal clinical benefit is achieved when molecular diagnostic guided therapy is introduced first-line, and not in relapsed or refractory cancers as in the current version of IMPRESS-Norway.

We are optimistic that these initiatives and technological advances will encourage both creative approaches and rigorous testing necessary to guide clinical practice. However, in

most cases, the improved clinical benefit will be incremental but still of significant importance for the patient. Through integrated efforts from multiple disciplines, the concept of precision oncology can continue to expand. ••

1. Flaherty et al., *J Clin Oncol* 2020;38:3883–94. PMID: 33048619

2. Konieczkowski et al., *Cancer Cell*. 2018; 33:801-815. PMID: 29763622

3. Ooft SN et al., *Sci Transl Med*. 2019; 11(513):eaay2574. PMID: 31597751

4. Neal et al., *Cell*. 2018; 175:1972-1988. PMID: 30550791

5. Helse og omsorgsdepartementet, Nasjonal handlingsplan for kliniske studier 2021–2025.

6. Rao et al., *JCO Clin Cancer Inform*. 2020; 4: 602-613. PMID: 32644817

7. van der Velden et al., *Nature*. 2019; 574:127-131. PMID: 31570881

CCBIO Opinion

Text: Eirik Joakim Tranvåg, CCBIO PhD Candidate

Evaluating personalized cancer drugs

Many countries with publicly financed health care have established systems for evaluating new drugs for reimbursement, with the Norwegian New Methods system and UK's National Institute for Health and Care Excellence (NICE) as well-known examples. These institutions have increasingly been criticized for applying evaluation methods that are not able to properly integrate central aspects of personalized medicine. Consequently, the Minister of Health and Care Services in Norway, Bent Høie, has ordered an evaluation of the New Methods system, with special emphasis on how personalized medicines are appraised. But why should the system change?

Before proceeding, a premise should be established: I take for granted that some sort of priority setting institution is desired to systematically evaluate these drugs before they are introduced into the public health care system. Not all countries have such a system, and it could perhaps be discussed whether this is at all needed. However, if controlling health care costs is an objective, I believe it is difficult to create a strong argument against drug reimbursement evaluations.

Why is it necessary to change how we evaluate personalized medicines? Because many drugs are rejected. Why are they rejected? Because the drugs are so expensive. And because their effect is not particularly strong. Thus, several papers have now documented that the average benefit from new cancer drugs approved by the EMA and FDA is modest and, in many cases, merely adds a few months of life. In addition to this modest benefit, the underlying evidence is uncertain. Increasingly, approvals are based on phase I and II studies, with fewer participants, short follow-up time and with surrogate endpoints that correlate poorly with patient survival or quality-of-life measures. As a result, more and more costly drugs with modest and uncertain benefits are appraised by the drug reimbursement system, and a proportion of these drugs are rejected. So why should the system change?

I agree that the system has to change. But not the system for reimbursement of new drugs. It is the system for research and development of new diagnostics and treatments that should change. It is unfair and unsustainable to develop new drugs with a mediocre impact on health, and price them as if they actually could cure cancer. It is unfair and unsustainable to fund basic research for drug development with public money and then having to pay for the drugs again when they enter the market. It is unfair and unsustainable that costly drugs demand increasing shares of the health care budget, with the harmful consequence that less resources are available to other needing patients.

Can universities and publicly funded research, like CCBIO, contribute to a more fair and sustainable system for research and development of new drugs? *Yes, we can*. Universities can establish guidelines and frameworks for socially responsible licensing, where affordable access to drugs built on publicly financed research is guaranteed. With such guidelines, a promising drug candidate developed by CCBIO could not be sold to big pharma without such guarantees.

And there would still be room for biomarkers. But they would need to be disconnected from new and expensive drugs. Biomarkers that predict toxicity or lack of response can prevent harmful treatment and save money by not providing treatments. Repurposing of drugs that are no longer protected by patents can be tested and tailored to new treatments for other patients. But most importantly, we as researchers must acknowledge that the current system of research and development is unfair, it has unsustainable consequences, and that the system has to change. ••

CCBIO Opinion

Text: Mark LaBarge, CCBIO International Faculty

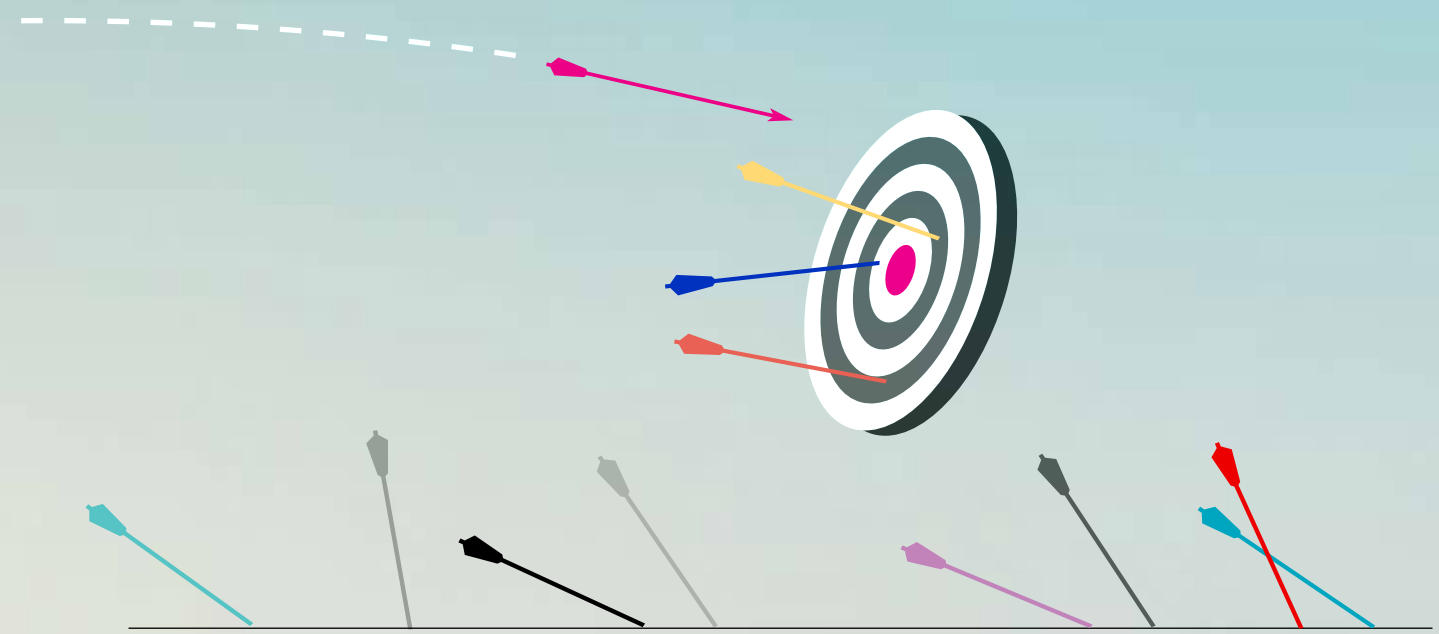
Challenges in breast cancer prevention

More than 80% of breast cancers in Norway, Western Europe, and the U.S. are diagnosed in women aged over 50. Although aging is generally associated with loss of function in tissues, age-related cancers may be paradoxical examples of gains of function; e.g. uncontrolled growth and the appearance of novel functions like invasion and metastasis. A long-held paradigm is that accrual of somatic mutations accounts for increased cancer incidence with age. Some cancers indeed show an exponential increase in incidence with age consistent with the accumulated mutation hypothesis, whereas the incidence of breast cancers in the U.S. decreases sometime after age 70. In addition, women from different countries, e.g. Japan versus U.S., exhibit completely different distributions for the age of first diagnosis, whereas accumulation of somatic mutations should be due to entropic forces that are experienced by all life on Earth[1]. Moreover, when normalized for incidence, most cancers are diagnosed after age 50, even chronic myeloid leukemias that can be driven by a single oncogene.

There is undeniably a genetic component to all cancers, however mutations alone are insufficient to explain the age-related increases of breast cancer incidence. A hypothesis that can encompass all of the observations that relate to aging and cancer is that increased cancer incidence results from gradual loss of function at the level of tissue structure and organization that corrupt tumor suppressive activity of normal tissue architecture, cause epigenetic changes that alters gene expression, thereby altering normal stem and somatic cell functions. These alterations lead to tissue-level phenotypes that make breast epithelia susceptible to cancer initiation. The hypothesis that accumulation of somatic mutations with age drives the age-related increase in breast cancer incidence, if correct, has a somewhat nihilistic conclusion; that cancers will be impossible to avoid. Alternatively, if microenvironment-driven epigenetic changes are key to explaining the tissue-level changes that make older women more susceptible to breast cancer, there is hope that primary prevention is possible[2]. Whereas genomes are nearly intractable to change, there is translational promise for altering the course of deleterious age-related tissue-level and epigenetic changes with therapeutic prevention, nutrition, and exercise[3]. Breast cancer prevention has fallen short so far, and there are practical and philosophical challenges ahead.

The standard of care for primary breast cancer prevention is screening by mammography, physical exam, and risk estimates based on Gail Scores. In high-risk scenarios (e.g. germline genetic risk or very strong family histories), prophylactic surgical modalities may be employed. Results from some exercise interventions suggest that more than four hours of weekly exercise may reduce risk, early pregnancy and breast feeding may also reduce overall risk, but these are not considered prevention modalities in a prescriptive sense. Indeed, therapeutic options for breast cancer prevention are limited. Selective estrogen receptor modulators (SERMs) and aromatase inhibitors are effective preventions because SERMs can reduce risk of recurrence by at least 30%. However, they are not for routine use in no-to-low risk patients, and compliance is bad due to side effects like deep vein thrombosis and bone loss.

Prevention clinical trials present philosophical and practical challenges that are less problematic in other types of disease intervention trials. Endpoints based on efficacy are impractical due to



the length of follow-up that is needed, and any molecule used as a putative prevention must be exquisitely safe because there is a strong case that doing nothing is likely to be as effective. A compromise to studying completely average-risk populations is to perform the intervention in high-risk populations who are more likely to progress to disease in a shorter time. In these populations, efficacy could be judged in a reasonable time, and a stronger argument can be made that these individuals are likely to benefit from an intervention. A compromise to efficacy is to examine endpoints that determine if an intervention exerts a biological activity indicative of a desired change in the breast within a shorter window of time: e.g. epithelial-cell proliferation, breast density, estrogen concentrations in tissue, and Masood scores.

There are a handful of trials in the U.S. testing chemical therapeutic interventions in high-risk populations that did not explicitly target hormone receptors or aromatases. Celecoxib treatment for six months was associated with a decreasing trend of breast density but no differences in Ki67+ cells (NCT00291694). Omega-3 treatment for six months in pre-menopausal women was associated with modest decreases in Ki67+ cells and Masood scores (NCT01252290). Vitamin D had no biological impact in breast tissues (NCT01224678). Genistein treatment in pre-menopause high risk women for six months did not affect proliferation, but lowered estrogen concentration compared to placebo (NCT00290758). Sulforaphane from broccoli extract had no effect after two weeks of treatment (NCT00982319). Therapeutic intervention-based prevention trials that are still recruiting, but have not reported outcomes, include: hydroxytyrosol in olive oil (NCT02068092), rapamycin (NCT02642094), omega-3 FA (NCT02295059), denosumab (NCT04067726), and metformin (NCT01905046). Whereas SERM use is associated with early biological impacts such as reduced Ki67+ cells and decreased breast density, most other interventions have shown minimal biological effect by the commonly applied outcome measures. We interpret this as either most of these non-SERM agents having minimal biological impact in breast, or that the wrong endpoints are being assessed.

Breast cancer prevention has been led by epidemiology, which is heavily influenced by what we can measure, or can think to measure. The associations that have been revealed between age, hormone receptors, and incidence are incontrovertible. However, the lack of success in translating those findings into durable cancer prevention strategies suggests that we must go deeper into the underlying biology of aging to understand and manipulate our susceptibility to breast cancer, as well as to identify the most telling biomarkers for prevention studies. ••

1. Todhunter, M. E., Sayaman, R. W., Miyano, M. & LaBarge, M. A. Tissue aging: the integration of collective and variant responses of cells to entropic forces over time. *Curr Opin Cell Biol* 54, 121-129, doi:10.1016/j.ceb.2018.05.016 (2018)

2. LaBarge, M. A., Mora-Blanco, E. L., Samson, S. & Miyano, M. Breast Cancer beyond the Age of Mutation. *Gerontology* 62, 434-442, doi:10.1159/000441030 (2016)

3. Fresques, T. et al. Breast Tissue Biology Expands the Possibilities for Prevention of Age-Related Breast Cancers. *Frontiers in cell and developmental biology* 7, 174, doi:10.3389/fcell.2019.00174 (2019)

CCBIO Opinion
Text: Yamila Torres Cleuren, CCBIO Research Advisor

CCBIO on Career Development

Young researchers face an enormous uphill struggle when it comes to taking their next career steps, having an overwhelming number of decisions to make even years before the time comes. "What comes after a postdoc? How and when can I become a PI? How can I build my own research group? Should I move location?" are just a few of the big questions they have. One major complication is a wide range of career paths and structures across universities and countries. Academic careers have become dynamic systems that are continuously changing – trying to adapt to the needs of the institutions and the society. With its established network of researchers, world-wide expertise, and resources, CCBIO is in a unique position to help its next generation get ready.

The current situation in Norway

A recent study by NIFU (Nordic Institute for Studies in Innovation, Research, and Education) showed that only one in five postdocs at Norwegian universities have become associate or full professors within five years after their postdoctoral period ended[1]. This is despite qualifying for faculty positions being the institutions' declared main goal of postdoctoral positions. Even more surprising: half the postdocs have left academia within five years after their postdoctoral period is over. This report comes after many years of debate into the use of postdoctoral positions and what it should mean to do a postdoc. A postdoc is not just a continuation of a PhD, and a postdoc should not be "just another researcher". During their postdoctoral periods, researchers are supposed to acquire the skills and tools needed to make their next career steps, whether that is inside or outside of academia. However, postdocs all around the world struggle to turn their temporary positions into full-time, stable careers[2].

Climbing the ladder: what should you do during your postdoc?

Most postdoctoral researchers in Norway reported of lacking a career plan and proper follow-up of their progress. While some researchers proceed to have successful careers outside of Norway, others struggle to make it within their Norwegian home institutions. What should you do during your postdoc? You will hear many answers to this, but most likely: everything! That is a daunting task. Your main priority should be on your research activities while increasing your independence, developing your own ideas, showing seniority in publications and collaborations. Generally, first- and last author publications are a must, and then come the "other tasks" you should embark on. From the start of your postdoc, you should get an overview of the skills, teaching, supervisory, (international) networking, and funding application and acquisition experience expected by the end of your postdoctoral period.

While planning for your career, you should always consider the possibilities at your home institution. Could you become a (co-)supervisor for master students and PhD candidates? Could you gain lecturing experience? Can you apply for your own funding or co-apply? The University of Bergen provides its junior researchers with

these opportunities, but many do not know that these options are available to them.

CCBIO's policy on career development
CCBIO wants to ensure that the next generation of researchers have the tools they need to make the right decisions when it comes to their careers. In addition to the already comprehensive stimuli from the CCBIO Research School for Cancer Studies, we are therefore introducing the CCBIO Masterclass Program (see separate chapters on both) where up to 10 post-PhD researchers will participate each year and receive mentorship, guidance, and training. During their one-year Masterclass period, the candidates are encouraged to discuss their career paths widely and to review their course and aims throughout the process. CCBIO thereby aims to motivate and challenge the participants. But most of all: we aim to facilitate their climb to the top. ••

1. Lang vei til toppstilling for postdoktorene, *NIFU*, https://www.nifu.no/news/lang-vei-til-toppstilling-for-postdoktorene/

2. Uncertain prospects for postdoctoral researchers, *Nature*, https://www.nature.com/articles/d41586-020-03381-3

IMPACT – TOWARDS A MORE DYNAMIC APPROACH TO CANCER

CCBIO performs research on cancer biomarkers along the entire chain from studies of basic biological mechanisms to diagnostic applications and clinical trials of novel therapy. Thus, the ultimate purpose of our endeavor is to improve the quality and cost-effectiveness of cancer treatment. As we have previously suggested, our contribution to that purpose cannot be robustly measured on the short term, for a variety of reasons. During the second term of our CoE – a Norwegian Centre of Excellence – we increasingly focus on how our research can be translated into lasting effects in cancer management, and how we can define sustainable metrics for such outcomes.

We have witnessed a year in which a single infectious disease, COVID-19, got more public and governmental attention than any other issue. As the panic hopefully retreats with the roll-out of vaccines, it is important to remind our citizens and the government that cancer is the major cause of premature death in a country such as Norway. Not even our worst scenarios of poorly managed COVID-19 would have changed that fact. Better prevention and better treatment for current poor responders to cancer treatment would have a strong long-term impact on general public health in our country.

In spite of strong research environments and a strong economy, Norway is not world-leading in terms of abundance of clinical trials. This is also the case with respect to cancer trials. National initiatives have been taken the latter years to improve on this situation, including a dedicated Action Plan from the Government, the infrastructure NorCRIN, and the governmental initiative NorTrials. Bottom-up, researcher-led initiatives are also developing.

CCBIO being a Centre of Excellence, our approach is to focus on translating our key scientific ideas into the Norwegian ecosystem of clinical trials. CCBIO was created on the recognition that cancers are systems diseases that involve causal pathways and regulatory networks in the tumor microenvironment at local and distant locations or niches. These multidirectional communications involve different hierarchical levels (molecules, cells, tissues, organs, organism). These complex functional patterns imply that genes and genomics are not sufficient as a research focus to improve on the present challenges with poor responders.

Additional ideas are needed, and they are to be found in functional diagnostics that can follow the more dynamic aspects of cancers in real time. For this reason, we have invested heavily in advanced methodologies such as single-cell and cell signaling analysis, multiplexed immunohistochemistry and multimarker imaging mass cytometry during our second CoE period. Our vision is that such methodologies can be integrated into routine cancer management to make therapy more dynamic and more adaptive. In this way, one can meet the needs of more of those who respond poorly by today's approach.

What CCBIO can deliver as a Centre of Excellence, is the scientific basis, proofs of concept along with visions and plans for further translation and exploitation of our work. Immediate impact will not miraculously emerge from CCBIO; however, it will have to be made by more hard work. We look forward to furthering the CCBIO vision in adaptive formats and contexts.••

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 scientific matters. Usually, the SAB convenes once a year for a full day meeting with CCBIO's investigators, mostly in connection with the CCBIO Annual Symposium. The feedback from the SAB has been of great inspiration and utility to CCBIO. Preceding every SAB meeting, CCBIO provides the SAB a report on its response to their previous recommendations. Due to the pandemic, the SAB was not able to convene in 2020 and will meet again in the spring of 2021.

> ***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.***

In their last report, the SAB stated that they were impressed by the progress made. CCBIO has developed into a strong center that is driving biomolecular marker research in Norway. The SAB noted particular strength in translating basic data into clinical studies and ongoing trials. CCBIO therefore recommended to put focus on clinical trials and on the usefulness of biomarkers that have either been derived from basic research performed within CCBIO or from the current literature.

The SAB also commented that a noticeable team spirit has been built, enhancing 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. They commended the 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, which 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 efforts 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. They consider the activities established in interaction with the Vascular Biology Program at Boston Children's Hospital to have contributed significantly to this end. ••

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

Ate van der Zee is professor of gynecological oncology and chairman 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 2020

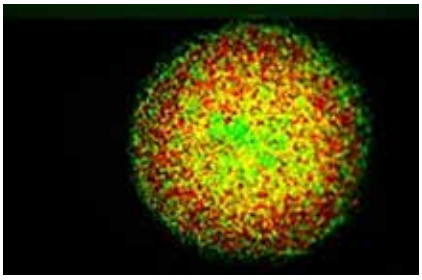
CCBIO has a two-arm portfolio of biomedical (Team 1-3) and societal (Team 4) projects. The Centre has a focus on biomarkers of tumor-microenvironment interactions in primary and metastatic cancers, including the expanding field of tumor immune biology, and how these features can define aggressive tumor phenotypes and predict tumor progression and response to therapy. Studies on ethics and economics represent an integrated and supporting part of CCBIO. All activities are performed in the context of interactive education and communication efforts.

During 2020, the COVID-19 pandemic has influenced our activities significantly. Laboratories have overall been running with reduced capacity, and this has caused delays for researchers at different levels. After the initial shut-down phase, courses and meetings were converted to online events with much success and significantly increased attendance nationally and internationally. It seems obvious that many lessons are to be learned from the COVID-19 experience, not only related to the disease itself and how it is handled, but also on how this disease has made us rethink and reinvent the ways we are communicating and working. As of today, we do not know how this will unfold during 2021. Still, we look forward to reconnect and restart our daily activities at full scale.

The **CCBIO Research School for Cancer Studies** has continued to increase its activities. We now have 9 basic courses, and three more are being planned, on clinical trials, innovation, and patient involvement in medical research. A strategic collaboration has been developed with the research school at Neuro-SysMed, a RCN funded Centre for Clinical Treatment Research (FKB) at Haukeland University Hospital and the University of Bergen. We believe that this move will benefit both centers. The CCBIO Masterclass Program for career development was launched, and CCBIO received its second INTPART grant from the RCN for developing further the relationship with the Vascular Biology Program at Boston Children's Hospital and Harvard Medical School. The very successful two-day Scientific Writing Seminar was repeated in 2020 with close to 300 participants.

In **TEAM 1**, projects are focusing on how tumor cells interact with and instruct the surrounding tumor microenvironment, by influencing key drivers such as immune responses, angiogenesis, cancer associated fibroblasts, and matrix involvement, favoring tumor growth and metastatic spread, and explaining development of treatment resistance.

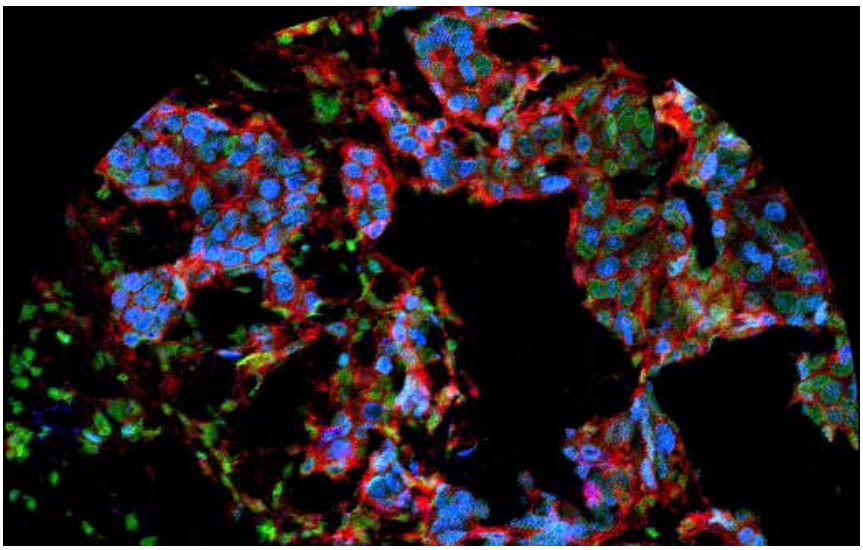
The **Gullberg group** has been working on fibroblast biology and the characterization of novel integrin α11 function blocking antibodies and development of a mouse model to explore the role of α11 in tumor stroma. In 2020, the group reported that the cytoplasmic tail of α11 plays a role in cell proliferation and cell migration, indicating that the importance of integrin α-chains in modulating classical β integrin chain functions might have been underestimated (Erusappan et al, Sci Rep 2020). The long-term project (started 2013) to generate an ITGA11-Cre mouse strain was completed and is now ready to move to the next level (Alam et al, Matrix Biol Plus 2020).



In the **Kalland group**, focus has been on two strategies: drug discovery by repurposing, and the concept of cryoimmuno-based dendritic cell therapy. During 2020, a phase I clinical trial for cryoimmuno-therapy (CryoIT) for patients with advanced prostate cancer was completed (Thomsen et al, in revision). Treatment effects were

suggested according to radiology, circulating tumor cell enumeration, large-scale serum auto-antibody profiling and ultradeep T-cell receptor sequencing. The planning of the next CryoIT clinical trial is ongoing. By functional assays and genome-wide profiling of monocyte-derived dendritic cells, a potential for more robust production of therapeutic pro-inflammatory dendritic cells was presented (Azeem et al, Front Immunol 2020). In further work, the role of beta-catenin and STAT3 signaling in dendritic cell re-programming will represent an important area.

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, and pancreatic cancers. Several imaging techniques have been studied, for example against CD24 (a stem cell and poor prognosis biomarker) in high-grade ovarian cancers in PDX-models, aiming for increased sensitivity in tumor detection and more precise surgery (cytoreduction). Strategies for improved drug delivery have been examined, for example by using sonoporation, showing how this might impact intracellular signaling of cancer cells with identification of biomarkers. During 2020, the team has reported the development of targeted fluorescent imaging that can be employed for tumor detection in PDX models of high-grade serous ovarian cancer (HGSOC) non-invasively (Kleinmanns et al, EBioMedicine 2020a). This approach was further developed to significantly improve the detection and resection of HGSOC with fluorescence image guided surgery in PDX models. Results demonstrated a 50% increase in the number of tumors detected and greatly improved extent of cytoreduction (Kleinmanns et al, EBioMedicine 2020b). Furthermore, progress was made in a project focusing on profiling of the

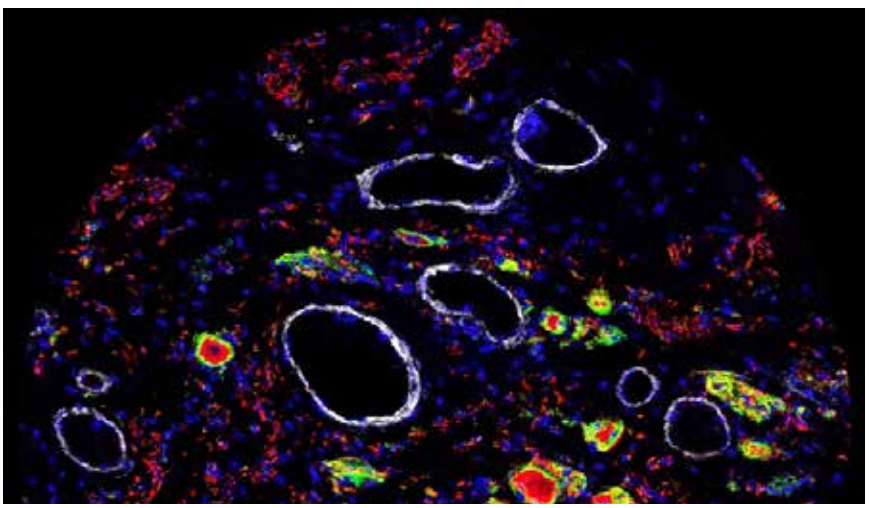


tumor immune microenvironment in human ovarian cancer by imaging mass cytometry.

In **TEAM 2**, studies are being performed on biomarker discovery and validation in several tumors, 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. Candidate biomarkers are used to map tumor diversity including associations with clinico-pathologic phenotypes and patient outcome.

The **Akslen group** is currently working on tissue biomarkers of the tumor microenvironment in human breast cancer, for improved understanding and more precise prognostication and prediction of treatment response. The main focus is currently on protein profiling of luminal-like and basal-like tumors. Three questions are asked: 1. How do the tumor proteome react to hypoxia in breast cancer subtypes? 2. Do neurogenesis in breast cancer differ between molecular subtypes, and is this phenotype coordinated with angiogenesis and immune response? 3. What are the roles of Nestin and Stathmin in aggressive breast cancer? Imaging mass cytometry (IMC) is used to map the cancer tissue landscapes for high-order co-expression patterns and delineation of tumor microenvironment niches. During 2020, the group reported novel findings on the role of Stathmin for vascular and immune responses in breast cancer (Askeland et al, Sci Rep 2020).

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. During 2020, the team reported that Axl is a driver of stemness in normal mammary gland and breast cancer (Engelsen et al, iScience 2020). The group also showed that Axl is a key factor in acquired resistance to EGFR targeted treatment in lung cancer (Lotsberg et al, J Thor Oncol 2020).

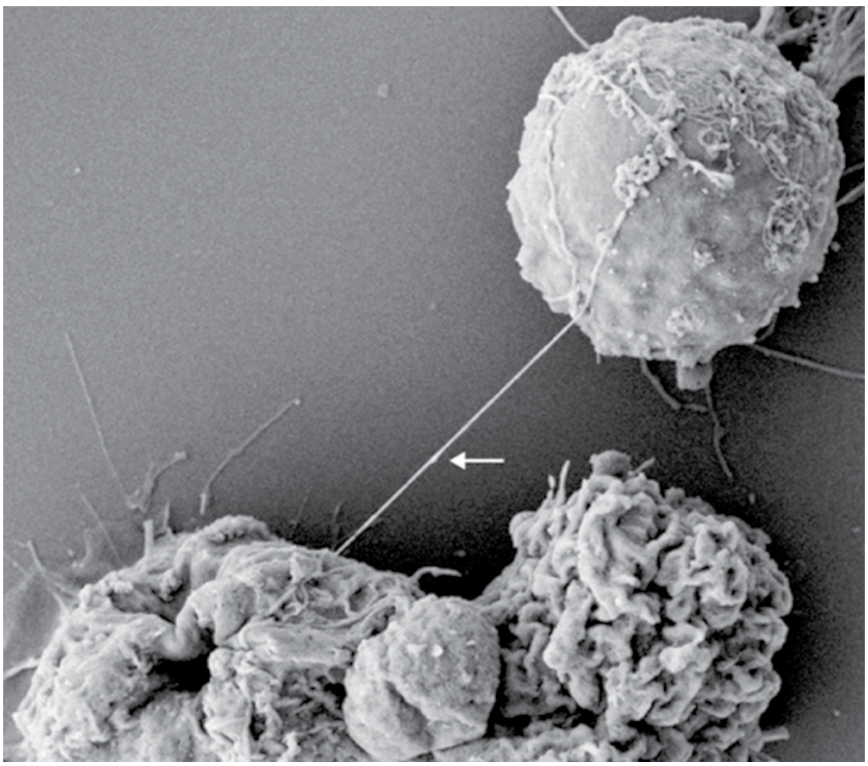


The **Costea group** studies tumor-stroma interactions in oral and vulvar squamous carcinoma, with focus on metabolic reprogramming of carcinoma associated fibroblasts (CAFs), and the association with genetic alterations including HPV subtypes and their role for tumor progression. The group also studies the role of the tumor stroma in drug resistance. During 2020, the group reported how metabolic reprogramming of normal oral fibroblasts correlated with increased glycolytic metabolism of oral squamous cell carcinoma and preceded their activation into carcinoma associated fibroblasts (Zhang et al, Cell Mol Life Sci 2020).

In studies of gynecologic cancers by the **Krakstad group**, tissue- and serum-based biomarkers are being 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 coordinated by the group. Novel models for endometrial cancer are being established and characterized, and integration of molecular and radiologic data with clinical phenotypes is ongoing. During 2020, the group reported on the development of prediction models for lymph node metastasis in endometrioid endometrial carcinoma (Berg et al, Br J Cancer 2020), and also on maintained survival outcome after reducing lymphadenectomy rates and optimizing adjuvant treatment in endometrial cancer (Forsse et al, Gynecol Oncol 2020). In relation to tumor immune responses, the team reported a high degree of heterogeneity of PD-L1 and PD-1 from primary to metastatic endometrial cancer (Engerud et al, Gynecol Oncol 2020).

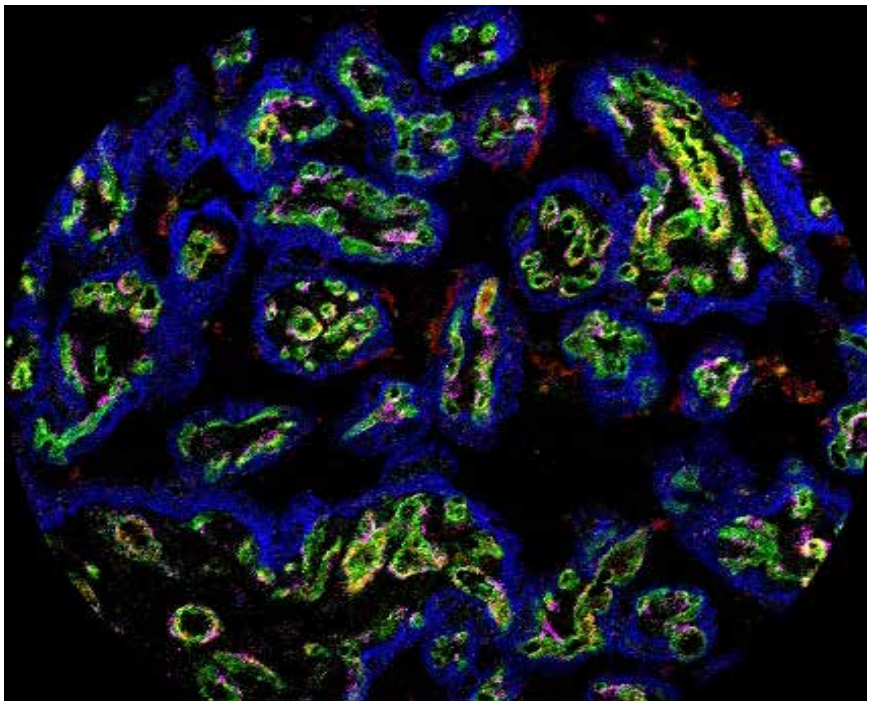
The **Wik group** has a focus on breast cancer of the young and why these patients often experience a more aggressive disease behavior. A large cohort has been established with multiple molecular and clinico-pathologic annotations, including primary tumors and metastases, and further genetic and imaging mass cytometric profiling is ongoing. So far, studies have been performed on estrogen related signaling networks and transcriptomic profiles with particular attention to tumor proliferation in aggressive patient subgroups. Wik is the director of the CCBIO Research School for Cancer Studies and is the local coordinator of the CCBIO-INTPART collaboration with the Vascular Biology Program at Boston Children's Hospital and Harvard Medical School. During 2020, a smooth transition to a digital format for the CCBIO PhD courses took place, including a novel collaboration with EMBO on graphical design. An educational collaboration between CCBIO and Neuro-SysMed (FKB) has been initiated.

In **TEAM 3**, 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 working on single cell biomarker profiling of leukemia and solid cancer cells and immune cells following treatment with conventional and novel targeted therapy in a trial setting, to stratify between responders and non-responders as early as possible. 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 team is active in the p53 field, with particular attention to the biological and practical importance of p53 isoforms. During 2020, the team presented results on various treatments and their effects on tunneling nanotube (TNT) formation and cell adhesion in chronic myeloid leukemia (CML) cell lines, suggesting a completely new therapeutic mechanism (Omsland et al, FASEB J 2020). Also, results on single cell detection of the p53 protein by mass cytometry were reported (Fagerholt et al, Cancers 2020).

The **Straume group** is focusing on tissue biomarker studies in clinical trials. The group has reported an 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. This work has been ongoing, although inclusion of patients was paused in March 2020 until September 2020.

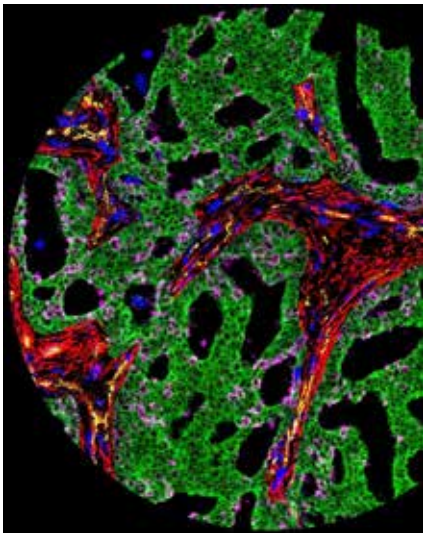
The **Bjørge group** is engaged in novel multicenter trials with translational research programs related to high-grade ovarian cancer. The group also has a focus on improved imaging guided cytoreduction surgery in this disease. In addition to clinical studies, PDX models and organoid cultures are being established. High-dimensional tissue profiling of ovarian cancer samples have been initiated with special attention to immune responses. During 2020, Bjørge and colleagues reported on CD24-targeted intraoperative fluorescence image-guided surgery leading to improved cytoreduction of ovarian cancer in a preclinical orthotopic model (Kleinmanns et al, EBioMedicine 2020).

In **TEAM 4**, 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 on 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 (Responsible Research and Innovation). and the coproduction of science, technology and society.

The **Strand 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 . The ELSA group of CCBIO interact with and are tightly linked to similar ongoing RRI projects (NFR Res Publica and AFINO, and Horizon 2020 SuperMoRRI and TRANSFORM). In 2020, the group enjoyed a major strengthening with the inclusion of Professor Marta Bertolaso as Adjunct Professor and a formalization of the collaboration with Bjørge's group. The team will search for further synergies with the Centre for Digital Life Norway, which has a strong RRI profile and of which CCBIO is an associated partner.

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 CCBIO-funded PhD projects by Kelly Mikyung Seo (cost-effectiveness modelling of predictive biomarkers in targeted oncology therapies) and Ana Beatriz D'Avó Luís (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 (accepted for publication), 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 2020, Kelly Seo was awarded her PhD by the London School of Hygiene and Tropical Medicine for her thesis titled "Economic evaluations of companion cancer biomarkers for targeted therapies". Dr. Seo reviewed methodological approaches and biomarker characteristics considered in existing economic evaluations. She also developed a practical guide to modeling the cost-effectiveness of companion biomarker tests. The thesis by Ana Beatriz Luís titled "Essays on Economic Incentives and Implications of Biomarker Tests" was accepted for defense at UIB in 2020 (and successfully defended in early 2021) (supervised by Tommy Gabrielsen and Julie Riise, UIB). The third candidate in cancer economics, Jiyeon Kang is now mid-way through her PhD (at LSHTM) titled "Improving economic evaluation and decision-making for oncology drugs using real-world data". She has built a unique database of 163 oncology appraisals undertaken by the UK-based National Institute for Health and Care Excellence (NICE), drawing on the evidence submission made by manufacturers, the independent report of the Evidence Review Group, and the final guidance issued by the Appraisal Committee. She is now developing methods by which to test a series of hypotheses regarding the use and acceptability of real-world data in these appraisals.

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 2019-2020, 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. The paper "Precision Medicine and the Principle of Equal Treatment: a Conjoint Analysis" (Tranvåg et al, 2020) won the 2020 Early Career Researcher Prize, sponsored by the Wellcome Trust, for the European region at the World Congress of Bioethics (June 2020). The article is based on a survey among Norwegian medical oncologists (in submission).

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 2020, several such projects have been ongoing, like the ERAPerMed project "AML_PM - Improved treatment of Acute Myeloid Leukemia" (with Gjertsen). Postdoc Dimitrios Kleftogiannis, linked to this project, is also using part of his time to work on breast cancer profiling with the Akslen and Wik groups in CCBIO. Within the AML_PM project, the team 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. In the fall of 2020, a new postdoc was hired to work on development and use of methods to exploit the Imaging Mass Cytometry (Hyperion) technology to the study of tumor-microenvironment interactions, in collaboration with the Akslen group. Current work includes establishing pipelines and designing analysis approaches for data sets to be generated within CCBIO.

Altogether, a range of research projects and communication activities 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 (now preparing the second editions of both volumes), several educational activities are being performed by the CCBIO Research School for Cancer Studies. Notably, the CCBIO Masterclass Program was launched in 2020, aiming for targeted teaching and training of young investigators aiming for independency and future positions as group leaders. We continue to reflect on the core concepts and integrated activities of CCBIO and the challenging transition to real life impact. ••

Research Programs

Teams 1-4

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 1**), exploration and validation of cancer biomarkers in human tissues **(Team 2)**, clinical studies and early trials **(Team 3)**, and societal studies including projects on ethics, economics and priorities **(Team 4)**. These four programs are supported by resources on bioinformatics and processing of big data, coordinated by Inge Jonassen, and Rolf Reed is a strategic advisor. Increased connectivity and collaboration within CCBIO have taken place over the years. CCBIO is supported by an International Faculty of 14 top scientists in different fields.

1

Mechanisms of Tumor-Microenvironment Interactions

The aim of this program is to examine how tumor cells interact with the surrounding tumor 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.

DONALD GULLBERG

Research focus
The research in the Gullberg group is focused on work related to the function of integrin α11 in tissue fibrosis and in the tumor microenvironment. The CCBIO projects deal with understanding the role of integrin α11 at the molecular and cellular levels in order to ultimately reach a better understanding of its role in the tumor stroma.

Subprojects
1. One focus of the CCBIO-supported activities 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). Characterization of functionality of Cre-recombinase in this mouse strain has been determined by crossing with the Rosa26R reporter strain. The first publication with this novel mouse strain was published in 2020 in Matrix Biology Plus (Alam J, et al. Characterization of an integrin ITGA11-Cre mouse strain with Cre recombinase expression restricted to fibroblasts. Matrix Biol. Plus. 2020).

2. A second project relates to the role of integrin α11 in squamous cell carcinoma (SCC) and is performed in collaboration with Ritva Heljasvaara, University of Oulu. Focus is on analyzing the role of dermal stroma in a mouse model of SCC using a mouse strain deficient in integrin α11.

3. A third project was initiated in 2020 and is performed in collaboration with Daniela Costea and will involve studies of integrin α11 regulation in cancer-associated fibroblasts (CAFs) by mechanical stiffness and use of Imaging Mass Cytometry (Hyperion platform) to visualize CAF biomarkers in the tumor microenvironment.

Important results
The group has generated the first transgenic mouse strain where an integrin promoter drives Cre-recombinase. Epitope mapping on integrin α11 function-blocking antibodies is ongoing.

Current challenges
Securing more research funding for basic research.

Focus and research aims in the coming years
The overall goal is to continue characterization of integrin α11 to be able to evaluate its potential as a therapeutic target.

Specifically, the group is:
1. Crossing ITGA11-Cre mouse strain with the double-fluorescent ROSAmT/mG reporter strain (Gt(ROSA)26Sor$^{tm4(ACTB-tdTomato,-EGFP)Luo}$, https://www.jax.org/strain/007576) which will enable direct visualization of the dynamic α11 expression in tissues and tumor stroma without fixation or other treatments.

2. & 3. Aiming to elucidate the molecular mechanisms explaining the effect of mechanical strain on integrin α11 expression and function, at the molecular level (2), and using the model of squamous cell carcinoma (3). ••

GROUP MEMBERS:

Gullberg, Donald, PhD, professor, group leader
Kusche-Gullberg, Marion, PhD, professor
Alam, Jahedul, MS, PhD candidate
Disha, Nazia Islam, master student
Goni, Osman, master student
Grønning, Mona, chief engineer
Lu, Ning, PhD, senior laboratory engineer
Moses, Musiime, MS, PhD candidate

KARL-HENNING KALLAND

Research focus
Kalland's group pursues a drug discovery and development program and dendritic cell-based cryoimmunotherapy (CryoIT) against cancer.

Subprojects
1. 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 a 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.

2. CryoIT: The phase I clinical trial has been completed with follow-up of all patients in 2020. 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
1. Drug Discovery and Development: The group's repurposing strategy has previously published two compounds which inhibit β-catenin signaling in cancer cell lines. The molecular targets and mechanisms were identified. The repurposing strategy has identified three novel compounds with STAT3-inhibiting activity. One of the compounds exhibited dual inhibition of both androgen receptor (AR) and STAT3. Patent applications have been submitted and licensing is negotiated with Xennials Therapeutics, Chicago, IL, USA, by Vestlandets Innovasjonsselskap (VIS).

2. CryoIT: The phase I clinical trial was completed for 18 patients with metastatic castration-resistant prostate cancer. 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. The median overall survival time was 34.9 months for the patients who were treated with CryoIT. The median progression-free survival was 10.5 months, as evaluated based on three radiological methods (MRI, PET-CT and skeletal scintigraphy) and international criteria for tumor size (RECIST). Highly valuable experience has been obtained on both treatment aspects and optimized biomarkers that benefit current planning of next generation CryoIT. The European Patent Office has approved the patent application of CryoIT combined with intratumoral injection of an immune checkpoint inhibitor. A manuscript reporting the results of the clinical trial has been submitted for publication.

Current challenges
The main challenges will be: 1) Establish Good Manufacturing Practice (GMP)-grade production of therapeutic dendritic cells in Bergen for the next phase CryoIT clinical trial; 2) Revision of the CryoIT protocol with planning and funding of the next phase clinical trial; 3) Establish a new *in vivo*-mimicking *ex vivo* model of patient materials for new quality control tests of therapeutic cells and drug combinations.

Focus and research aims in the coming years
The overarching focus and aim will be to develop enhanced immunotherapy against cancer. The group envisages a next stage clinical BASKET trial during 2021-2024 and a next generation CryoIT trial protocol in 2024-25. The BASKET trial will include patients with prostate cancer, kidney cancer and vulvar cancer. The next generation CryoIT protocol will be enhanced by more robust and potent therapeutic dendritic cells. ••

GROUP MEMBERS:

Kalland, Karl-Henning, MD, PhD, professor, group leader
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Azeem, Waqas, PhD, senior engineer
Bakke, Ragnhild Maukon, Medical Student Research Program
Gabriel, Benjamin, PhD, researcher
Hoang, Hua My, research technician, UiB
Hua, Yaping, PhD, postdoc
Lellahi, Seyed Mohammad, PhD, postdoc
Nguyen, Rebecca, laboratory technician

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 with limited therapeutic options.

Subprojects
SonoCURE funded through the Norwegian Research Council, NIH and the Western Health Board explores the application of Sonoporation in the treatment of Pancreatic Ductal AdenoCarcinoma (PDAC). PreLIM funded by the Norwegian Cancer Society and H2020 (AML VACCiN) 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, funded through Helse Vest and a Marie Sklodowska-Curie innovative training network (ISPIC) INOvA, the group is developing the application of image-guided surgery, whereby fluorescent dyes will target biomarkers on surgically amenable cancers, to aid their greater resection. The group is planning studies in dogs in addition to starting human trials. Further research is dedicated to establishing an *in vitro* drug-screening organoid platform and to profile the tumor microenvironment of high grade serous ovarian cancer (HGSOC) patients using a mass cytometry panel to aid the identification of new biomarkers for personalized medicine.

Important results
The SonoCURE team demonstrated the impact of sonoporation with gas filled microbubbles on drug delivery to PDAC cells (Bjånes et al., Drug Metab Dispos 2020; Bjånes et al., Pharmaceutics 2020), studied intracellular signaling of cancer cells upon sonoporation and identified biomarkers that can be exploited for therapeutic intervention in combination with sonoporation (Haugse et al., Pharmaceutics 2020). Haugse and Bjånes defended their thesis in 2020. In addition, the team investigated the impact of different gas filled microbubbles on PDAC and finalized the NIH pre-clinical trial on selecting optimal sonoporation parameters (Kotopoulis et al.; Schultz et al.).

The PreLIM team have been involved in collaborative work that led to the identification of a new therapeutics target for mantle cell lymphoma (MCL) (Lazarian G et al., Oncogene 2020; Alshareef et al., Int J Mol Sci). Furthermore, the team has identified two small-molecule therapeutic targets for MCL. The team is in collaboration with Dr. Davila at the Moffitt Cancer Center for the development of new cell-based immunotherapy towards hematological malignancies and solid cancer (lymphoma-leukemia, ovarian cancer).

The INOvA team identified the tumor biomarker CD24 for the detection and resection of ovarian cancer tumor masses. CD24 is overexpressed in approximately 90% of ovarian cancer patients and in 68% of multiple other human carcinomas. Fluorescently labelled CD24 enabled real-time intraoperative identification of primary tumors and metastases in HGSOC OV-90^{luc+} xenograft and CD24 heterogenous expressing patient-derived xenograft (PDX) models; thus, identifying the use of a CD24 targeted contrast agent as a promising surgical debulking approach (Kleinmanns and Fosse et al. 2020).

Current challenges
The major challenge across 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 microenvironment has dramatically impacted the way preclinical research is developed and performed.

Focus and research aims in the coming years
The 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:
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Gelebart, Pascal, PhD, researcher
Langer, Anika, PhD, researcher
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Sand, Louise Bergsjø, MS
Tandaric, Luka, MS
Viñegra, Elvira García de Jalón, MS

Master student
Robert Willoughby

2

Discovery and Validation of Cancer Biomarkers

The aim of this program is to explore and validate different classes of biomarkers in tissue samples from human patient cohorts and clinical trials material. The investigators take advantage of the recently established technology of IMC (imaging mass cytometry) using panels of multiple biomarkers for simultaneous analysis of various tissue compartments in parallel with functional interrogation. The studies map associations with clinico-pathologic phenotypes as well as prognostic and potentially predictive properties. This team consists of the Principal Investigators Akslen (CCBIO director) and Lorens and their groups, and the Associate Investigators Costea, Krakstad, and Wik.


2

LARS A. AKSLEN

Research focus
The focus of Akslen's group has been to discover and validate novel tissue-based cancer biomarkers, especially related to the tumor microenvironment, for better biological understanding and improved prediction of aggressive tumor behavior. As part of precision pathology, such markers are expected to assist in molecular classification and grading of malignant tumors, to aid precise management of the patients. The group now concentrates on tumor proteomics (Mass Spectrometry) and multi-marker mapping of intact tumor tissues (Imaging Mass Cytometry; Hyperion platform).

Projects
1. Proteomics portraits of breast cancer subtypes, with particular focus on the tumor microenvironment.
2. Markers of neuro-angiogenic phenotypes in breast cancer subtypes, and associations with the tumor immune microenvironment.
3. Role of Nestin and Stathmin as markers of BRCA1-related and basal-like breast cancer, with particular focus on the tumor microenvironment.

Important results
Proteomic profiling of laser captured micro-dissected breast cancer tissues has been performed, separating the cancer cells 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 re-programming (Kjølle et al., in prep.).

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 differ according to basic clinico-pathologic characteristics and disease progression and might provide novel biomarkers and targets for more precise patient management (Wik et al., in prep.).

Expression status of Nestin (mRNA and protein), a candidate biomarker for aggressive breast cancer, was found to correlate strongly with basal-like and BRCA1-associated tumors, and 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 the angiogenic and immunogenic responses in the microenvironment of aggressive breast cancer (Askeland et al, Sci Rep 2020).

Current challenges
A major challenge in the field of deep tissue profiling is to account for the complexity and heterogeneity within malignant tumors. Future *in situ* studies need to improve information on spatial resolution. Mapping of cancer tissues with definition of cellular niches will increase the quality of *in situ* proteomics. This approach is assumed to improve the precision of diagnostic, prognostic and predictive signals as integrated parts of precision onco-medicine.

Focus and research aims in the coming years
In the Akslen group, projects will continue to explore the phenotypic diversity and complexity in breast cancer subtypes, with special focus on tumor-microenvironment niche architecture.
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JAMES B. LORENS

Research focus
In spite of significant improvements in cancer therapy, most cancer patients will not experience lasting benefit. Understanding why therapies fail and developing novel biomarkers and treatment paradigms to address these resistance mechanisms remains a central goal for cancer research. The Lorens group discovered that the receptor tyrosine kinase AXL is a key driver of acquired resistance to multiple cancer agents. By determining the molecular mechanism of AXL regulation on the tumor microenvironment, in concert with combination clinical trials with AXL targeting agents, a new paradigm to improve cancer treatment has emerged.

Subprojects and important results
1. AXL is a driver of stemness
The group demonstrated that AXL drives stemness and plasticity traits in cancer, and that is a co-option of a regulatory function normally reserved for stem cells. AXL is expressed in multipotent mammary epithelial stem cells (MaSC) and is required for mouse mammary gland reconstitution upon transplantation. An AXL-dependent MaSC gene signature is a feature of basal breast cancers and reduced patient survival, irrespective of subtype. Hence AXL regulates access to epithelial plasticity programs in MaSCs and, when co-opted, maintains acquired stemness in breast cancer cells that drive progression and drug resistance.

2. AXL in acquired cancer therapy resistance
All successful cancer therapies involve some degree of enhanced tumor immunity. As drug resistance evolves under immune surveillance, mechanisms that promote cell survival and immune evasion will be favored. The group found that EGFRi resistance in lung cancer was mediated by upregulation of AXL. AXL inhibition abrogated cytoprotective autophagic flux and induced immunogenic cell death in drug resistant NSCLC. The 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.

3. AXL in tumor-immune crosstalk
Tumor suppressive myeloid cells are a primary obstacle to immunotherapy. The group's recent results show that AXL targeting enhances immune checkpoint inhibitor efficacy by blocking both tumor EMT and suppressive myeloid cell mechanisms. The findings indicate that AXL signaling integrates cancer cell plasticity with immune suppressive myeloid mobilization and that tumor immunity can be enhanced by combined immunotherapy and AXL targeting.

Current challenges
Deeper understanding in the role of the tumor microenvironment (TME) during cancer initiation and progression is critical both to further cancer biology and as a source of improved molecular diagnostics and therapeutics.

Focus and research aims in the coming years
The group will focus on determining how AXL receptor signaling regulates acquired resistance to cancer therapy. The unique signal transduction of GAS6–AXL complexes will be studied using systems-level signal transduction analysis and high dimensional single-cell mapping of phenotypic-spatial features of the tumor microenvironment in preclinical models and cancer patient biopsy samples. ••

GROUP MEMBERS:

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Lorens, James, MS, PhD, professor, group leader
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Lu, Ning, senior engineer
Siraji, Muntequa Ishtiaq, staff engineer
Stigen, Endre, staff engineer

DANIELA COSTEA

Research focus
The research in Costea's group is focused on tumor-stroma interactions for identification of tumor microenvironment-related prognostic biomarkers.

Subprojects
- Mechanisms of tumor-stroma interactions including metabolic coupling.
- Understanding the role of tumor stroma in drug resistance.
- Stroma as a source of prognostic biomarkers.

Important results
Understanding how cancer cells control the energy balance in their microenvironment is vital for cancer treatment. Using stepwise models of carcinoma progression, the group has shown a continuous loss of mitochondrial activity and an elevated generation of L-lactate with tumor progression in carcinoma-fibroblast co-cultures. Furthermore, the fibroblasts were proven to be the main L-lactate producers, indicating that the main energy producer in a carcinoma is the stromal compartment (Zhang et al., Cell Mol Life Sci, 2020). The therapeutic importance of this result was shown by the finding that metabolically reprogrammed stromal fibroblasts were able to rescue carcinoma cells from the metformin-induced apoptosis through inhibiting the activity of AMPK and PARP and maintaining the mitochondrial membrane potential (Zhang et al., Cell Cycle, 2019). This indicate that metformin effects on cancer cells are modulated by the microenvironment and that this must be taken into consideration when developing a new combination of drugs for cancer treatment including metformin.

Together with Line Bjørge (Team 3), the group has investigated the role of fibroblasts for tumor formation and progression in vulva cancer. Results from both 3D organotypic models and xenograft mouse models showed a key role for stromal fibroblasts in carcinogenesis of lichen sclerosus associated vulva cancer (Dongre et al., Exp Cell Res, 2020).

As part of a national multicenter collaboration project, The Norwegian Oral Cancer (NOROC) Study, the Costea group participated in evaluation of several histopathological variables, including stroma-related parameters (Steigen et al., J Oral Pathol Med. 2020). A histo-score combining tumor differentiation and lymphocytic infiltrate identified a group of patients with particularly low survival among those in the low-stage disease (Bjerkli et al., Virchows Archiv, 2020). This suggests that a histo-score combining tumor differentiation and lymphocytic infiltration should be given special consideration in treatment planning of oral squamous cell carcinoma.

Current challenges
The group has shown that cancer associated fibroblasts are a heterogenous population of cells involved in a complex interaction with carcinoma cells, immune cells and endothelial cells. The challenge is to decipher these interactions at the molecular level, by using relevant experimental models that are sufficiently elaborated to mirror the complex *in vivo* tumor microenvironment 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.

Focus and research aims in the coming years
The group will focus on deep characterization of the fibroblasts' heterogeneity and their interaction with various subpopulations of cancer cells, inflammatory and endothelial cells by use of imaging mass cytometry (the Hyperion imaging system) as well as on developing robust *in vitro* 3D tumor models for dissecting tumor-stroma interactions at the molecular level and for high throughput drug testing. ••

GROUP MEMBERS:

Senior researchers:
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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 the establishment of improved model systems for endometrial cancer, to generate tools that enable functional studies and evaluation of biomarker expression in relation to treatment.

Subprojects and important results
1. Biomarkers for new therapy
It is a continuous focus for the group to assess promising biomarkers as well as clinical outcome in their population-based endometrial cancer cohort, including the relationship to changes in treatment management over time. During 2020, the group assessed the expression of PD-L1 and PD-1, suggested as predictive markers for immunotherapy and increasingly relevant in endometrial cancer. The reported fraction of positive primary tumors has been inconsistent, and the discrepancy between primary tumors and metastatic lesions has previously not been investigated. In a paper by Engerud et al., the group confirms that PD-L1 and PD-1 are frequently expressed in endometrial cancer, and expression patterns are similar across MSS and MSI tumors. In corresponding metastatic lesions, expression is inconsistent and variable compared to primary tumors, and this should be considered when treatment strategies are decided. More research is needed to identify patients who may respond to immune checkpoint inhibitors in endometrial cancer.

2. Effect of changes in treatment for endometrial cancer patients
In a publication by Forsse et al, the group focused on the main controversies in endometrial cancer treatment; the role of lymphadenectomy and optimal adjuvant treatment. A total of 1308 patients were included, all treated at Haukeland University Hospital over the two last decades. The study demonstrates that preoperative stratification by imaging and histological assessment permits a reduction in lymphadenectomy to around 50%, and is achievable without an increase in recurrences at 3 years. In addition, the findings support that adjuvant chemotherapy alone performs equally well to adjuvant radiotherapy with regard to survival and is likely superior in advanced stage patients.

Current challenges
The incidence of endometrial cancer is expected to rise due to its tight link to obesity and high age. Identifying specific patient populations that are likely to respond to therapy is therefore highly important. The introduction of texture analyses and machine learning have opened new possibilities for analyzing preoperative MRI and PET-CT data. Developing and exploiting radio(geno)mics to improve risk-prediction and diagnostics for endometrial cancer is of high interest. In addition, a key challenge is still to link molecular subgroups, often defined by the TCGA classification 3 to relevant treatment. Robust models that allow high-throughput screening is needed to test biomarker-guided targeted treatment.

Focus and research aims in the coming years
The group will continue to develop their molecularly defined models for endometrial cancer and use 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 platform. Developing relevant biomarker-panels for both stromal and tumor components is prioritized. They will also continue the strong focus on the MOMATEC2 trial and aim to complete this trial with the collaboration of the currently contributing centers, both nationally and internationally. An addendum to the protocol will allow for the sentinel node procedure alongside lymphadenectomy. ••

GROUP MEMBERS:

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ELISABETH WIK

Research focus
The research group Breast Cancer of the Young - Bergen (BCY-B) was established in 2019. The group's research focus is on breast cancer of the young, a group that experiences 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.

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

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

3. Age-dependent transcriptomic alteration 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 still in its early phases. One achievement is the establishment of a large clinical cohort of breast cancer of the young, including tissue material and histopathologic annotations, with long and complete follow-up data. The first paper from this cohort is in pre-submission phase (A. Svanøe et al.), and work on GATA3 and FOXA1, transcriptional age-dependent alterations, and molecular subtypes in metastases from breast cancer of the young, is in progress. Achievements in 2020 have been to initiate work on the Nanostring technology in the group, and successfully acquiring funding from Helse Vest for the period 2021-2023.

Current challenges
Integrating the multi-level omics and tissue data into meaningful, strong biomarkers is a challenge. Strong collaborations between multi-level researchers are required.

Focus and research aims in the coming years
The group plans to explore the tumor microenvironment with age-related biological differences in focus. Signature approaches are applied in biomarker development. Established methods such as imaging mass cytometry (Hyperion) and the Nanostring technology will be increasingly used. Validation and development towards clinical use, is an aim. 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

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Tegnander, Amalie Fagerli

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.


3

BJØRN TORE GJERTSEN

Research focus
The Gjertsen group focuses on intracellular signal transduction in conventional and targeted therapy. Clinical trials are chosen as a translational medicine approach and form the experimental framework to examine signaling in tumor cells and its relation to therapy response. The transcription factor and tumor suppressor p53 is selected as molecular integrator and nexus for the cancer related intracellular signaling.

Signal transduction is directly involved in leukemogenesis of more than 50% of the aggressive blood cancer acute myeloid leukemia (AML). This is reflected in a spectrum of recurrent mutations found in the progenitor cells, including RAS-genes, receptor tyrosine kinases like FLT3, c-KIT and CSF3R and tyrosine phosphatases. In contrast, chronic myeloid leukemia (CML) nearly always includes a BCR-ABL1 fusion where the ABL1-part comprise a leukemogenic tyrosine kinase. The group has established studies of CML analyzing specific inhibitors of ABL1 in trials, mouse models and *in vitro*. Kinase inhibitors have been compared with interferon alpha, the first promising therapy for CML and now explored in combination with kinase inhibitors for enhanced response and increased probability for cure.

Subprojects
Subprojects include single cell immune and signaling profiling of patients with CML, AML and selected solid cancers, using samples of peripheral blood from patients in clinical trials. The group's data indicate that CML responds homogenously to kinase inhibitors directed to their driver oncogene BCR-ABL1. Acute myeloid leukemia is a heterogenous stem cell disease, and preliminary data with the AXL inhibitor bemcentinib reflects this manifold genetic background. Lymphocytes in both leukemia and solid cancers may contain information of response to immune therapy, and this should be determined in detail.

The p53 research aims to examine if the p53 protein may form a ubiquitous biomarker of disease as well as an indicator of response. Ongoing work address how AXL and BCR-ABL1 may regulate the p53 protein in AML and CML.

Important results
Tumor-stroma interactions include inter-cellular communication through tunneling nanotubes, a recent mechanism of action.

Use of p53 analysis in single cell signaling profiles are accessible (Fagertun et al. 2020). Future studies will address p53 protein isoforms in targeted therapy, differentiation therapy and in the differentiation stage of leukemia.

Current challenges
An increasing number of highly active and expensive new medicines and advanced medicinal products are introduced in the market. Better methods to determine therapy responders is highly needed, avoiding unnecessary treatment and unnecessary toxicity.

Focus and research aims in the coming years
The group has worked to optimize and prepare collection of samples from various studies with mature clinical data. These experiments will be analyzed and reported in the coming two years, focusing on early detection of responders. These experiments will also create a solid foundation for the strategy of analysis of ongoing trials that will be completed in 2021.

The study of interferon alpha signaling in leukemia will be followed up from the basic study of tunneling nanotubes to patient responses in CML undergoing combination therapy with a kinase inhibitor and interferon alpha. Three clinical trials studying special combinations will be examined and searched for patterns of response, comparing the rare blast crisis transformations observed. ••

GROUP MEMBERS:

Researchers:
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Wangen, Rebecca, MS, head engineer

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.

Subprojects
1. Clinical trial: A phase Ib/II randomised open label study of BGB324 in combination with pembrolizumab or dabrafenib/trametinib compared to pembrolizumab or dabrafenib/trametinib alone, in patients with melanoma.

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 in the trial.

3. Clinical trial: Efficacy of bevacizumab monotherapy in treatment of metastatic melanoma and predictive value of angiogenic markers. Currently, stress response related biomarkers are in focus.

4. Clinical trial: Predictive markers of response to sunitinib in treatment of metastatic renal cell carcinoma. The goal is to analyze predictive markers.

5. Research project: Importance of physical trauma on time to recurrence after primary treatment of breast cancer. The project is based on the hypothesis that dormant micrometastases can initiate tumor growth following a systemic burst of growth factors after surgery or trauma.

Important results
65 patients have received treatment in the phase Ib/II randomised open label study of BGB324 as of January 2021. Five regional centers include patients. An interim analysis in February 2020 revealed a challenge regarding the balance between the experimental arm and the control arm in the patient population. Significantly more patients in the experimental arm were in high risk stage IV (M1c and d (60%)) compared with the control arm (30%). M-stage is a fundamental prognostic factor in melanoma with significant impact on patient outcome. Following the recognition of this imbalance, inclusion of patients was paused in March 2020 until September 2020. This coincided in time with the outbreak of the COVID-19 pandemic. During this period, the group investigated the randomization procedure and discussed whether changes should be made to restore balance between the groups. No flaws or protocol violations were detected. After thorough discussions, the group concluded to continue as planned with no amendments in the randomization procedure. Enrollment of patients restarted in September 2020. A new version of the study protocol is currently under review.

Two PhD candidates successfully defended their thesis in 2020, Martin Pilskog and Hanna Dillekås.

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. There is a 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.

Focus and research aims in the coming years
The group is currently in the process of designing a new phase 2 clinical trial in renal cell carcinoma combining cryoimmune therapy with immune checkpoint inhibitors. Two more clinical trials are under planning. Currently, the group has an increasing focus on the importance of different stress responses in physiologic downregulation of the normal defense against DNA damage, thus resulting in mutations that in turn encourage uncontrolled cell growth and the escape from tumor dormancy. The group wants to increase their efforts to investigate the biology behind these evolutionary conserved mechanisms and the role in cancer. ••

GROUP MEMBERS:

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


3

LINE BJØRGE

Research focus and subprojects
The understanding of the pathogenesis of high-grade serous ovarian carcinoma (HGSOC) is growing, and molecular (BRCA mutations, HR defects) and phenotypic (platinum sensitivity, degree of debulking) profiling is being integrated into clinical trials and wider practice. Introduction of PARP inhibitors to frontline treatment is believed to translate into an overall survival benefit. Further improvements will require rethinking, and an international 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).

In order to accomplish the vision, Line Bjørge has together with Emmet McCormack set up a research team named INOvA (Innovative Novel Ovarian cancer treatment Approaches) that works with and focuses on the various programs.

For vulva cancer, a rare disease where stroma determines the biological behavior and no effective treatment exists neither for local advanced radioresistant disease or systemic metastases, a similar research program as well as a multidisciplinary team is now being established together with Daniela Costea and Karl-Henning Kalland.

Important results
The group has established tools for deep-tissue profiling, a mouse xenograft model platform, near-infra-red (NIR) probes for tumor identification and early-phase studies with modern design. These discoveries represent the foundation for ongoing and future projects. The two-investigator initiated early-phase clinical study is still ongoing, but due to the pandemic, the recruitment has for periods been temporarily stopped. The PhD candidate Harsh Dongre successfully defended his PhD thesis work in 2020.

Current challenges
Based on the improved recognition of cellular and molecular diversity, a more refined personalized approach to research and clinical trials for both ovarian cancer and vulva cancer is needed. Roadmaps for research priorities have 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 the patients, recognizing how the disease itself, as well as the treatment, may interfere with the patients' overall wellbeing and quality of life is critical.

Focus and research aims in the coming years
Inherent tumor biological characteristics of HGSOC and vulva cancer influence the effect of different therapies (surgery, radiotherapy, chemotherapy, and targeted therapeutics). To be able 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 programs the group is establishing. Further, given the importance of surgery for both diseases, tumor targeted fluorescence-image guided surgery methodologies will be further developed.

Objectives:
1. To generate unique HGSOC and vulva cancer organoid platforms.

2. To integrate the use of single-cell profiling of well-defined clinical trial cohorts to define biomarkers and preclinical models (PDX models) that portray the *in vivo* activity of the study drug(s).

3. To develop sensitive and specific tumor-targeted NIR fluorescent agents for cancer detection during debulking surgery. ••

GROUP MEMBERS:

Bjørge, Line, MD, PhD, MBA, professor, group leader
Anandan, Shamundeeswari, MS, PhD candidate
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Enge, Elisabeth, study nurse
Fosse, Vibeke, DVM, veterinarian
Gissum, Karen Rosnes, MS, PhD candidate
Gjerde, Christiane Helgestad, MD, PhD candidate
Kleinmanns, Katrin, MS, PhD, postdoc
Le, Minh Thu, study nurse
Tandarić, Luka, MS, PhD candidate
Thomsen, Liv Cecilie Vestrheim, MD, PhD, researcher
Torkildsen, Cecilie Fredvik, MD, PhD candidate

4

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 to improved education of CCBIO scientists in this dimension of the 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.

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 small-scale operation that can be seen as one project. They interact and are tightly linked, however, to the similar ongoing RRI projects (NFR Res Publica and 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. In 2020, the group enjoyed a major strengthening with the inclusion of Professor Marta Bertolaso as Adjunct Professor and the formalization of the collaboration between the Bjørge and Strand groups, through the hiring of Karen Gissum as a PhD fellow.

Important results
Strand's group builds insights and intellectual understanding (for peers) and ELSA/RRI awareness, within the consortium and its partners and audiences. In 2020, a key focus was the analysis of the sociotechnical imaginaries of personalized and precision cancer medicine that are currently abundant in cancer research policy. A key result is that these imaginaries rest upon reductionist assumptions that are long refuted. The questions that follow are (1) Why are they still being reproduced? And (2) what would be the implications for more responsible cancer research policies and practices if its sociotechnical imaginaries better take into account critiques of reductionism? Both in philosophical and media studies, the group has accordingly searched for *re-framings* of cancer.

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, researchers have been challenged by policy to become relevant to practice and integrate their insights into the daily life of medical research – notably through policy concepts such as ELSA and RRI.

Focus and research aims in the coming years
The main short-term plan is to finalize the book project that was undertaken in 2020, with a synthesis of the insights from the group's collaborations within Team 4. In 2020, the group secured a contract with a leading academic publisher and drafted most of the chapters; in 2021 the volume will be submitted to the publisher.

CCBIO has entered its second 5-year period. Before 2023, the group's challenge is to create a level of ELSA and RRI 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.
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GROUP MEMBERS:

Strand, Roger, dr.scient., professor, group leader
Bertolaso, Marta, adjunct professor
Bremer, Anne (née Blanchard), PhD, researcher
Gissum, Karen, PhD candidate
Nilsen, Irmelin W, M. Phil., research assistant
Stenmarck, Mille Sofie, cand. med., guest researcher

OLE FRITHJOF NORHEIM

The Bergen Centre for Ethics and Priority Setting (BCEPS) was established in 2019 with funding from the Bill & Melinda Gates Foundation, the Trond Mohn Foundation, Norad and the University of Bergen. In 2020, BCEPS has established its main area of activities in Ethiopia, Zanzibar. Malawi, and Norway. With COVID-19, BCEPS has been a particularly active contributor to research and decision support for priority setting and fair allocation of vaccines. In addition, the collaboration with CCBIO on cancer biomarkers, precision medicine and fair priority setting has continued as before.

Research focus
The aim of CCBIO is to discover, validate and translate cancer biomarkers, a key component of precision medicine. Norheim's team is interested in how cancer biomarkers can inform and 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 PhD project investigating how cancer biomarkers inform treatment recommendations for new and expensive cancer drugs is approaching finalization. Two different empirical studies are central: 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 Nye Metoder, the Norwegian drug reimbursement system.

In addition, the team works with the CCBIO ELSA team on a chapter for the forthcoming book. Here, they investigate the ethical challenges emerging when using biomarkers to stratify larger patient groups into smaller and more personalized sub-groups.

Important results
The paper "Precision Medicine and the Principle of Equal Treatment: a Conjoint Analysis" won the 2020 Early Career Researcher Prize, sponsored by the Wellcome Trust, for the European region at the World Congress of Bioethics in June 2020. The article is based on a survey among Norwegian cancer doctors and is awaiting review in a peer reviewed journal.

Current challenges
The increasing amount of new and expensive cancer drugs entering the market offer opportunities, but also challenges. With often marginal effects and unreasonable and confidential pricing, these drugs will impose a heavy burden on our publicly financed health care system.

Focus and research aims in the coming years
The team will continue the work on priority setting at both clinical and policy levels. A couple of very interesting papers from the PhD project will be published in 2021. The BCEPS team will also continue to contribute to the ELSA team's important work to create awareness of the ELSA-related areas in CCBIO. The aim is to continue the good dialogue and exchanges with other CCBIO researchers and clinicians. ••

GROUP MEMBERS:

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


4

JOHN CAIRNS

Research focus
The Health Economics Group have a primary focus on obtaining a better understanding of the cost-effectiveness of cancer biomarkers and of decision making regarding the adoption of new cancer therapies.

Subprojects
Kelly Mikyung Seo was awarded her PhD by the London School of Hygiene and Tropical Medicine for her thesis entitled Economic evaluations of companion cancer biomarkers for targeted therapies in November 2020. She reviewed methodological/modeling approaches and biomarker characteristics considered in existing economic evaluations and conducted a cost-effectiveness analysis of a novel biomarker (HSP27 expression). She then went on to develop a practical guide to modeling the cost-effectiveness of companion biomarker tests.

Jiyeon Kang is now mid-way through her PhD entitled Improving economic evaluation and decision-making for oncology drugs using real-world data. She has built a unique database of 163 oncology appraisals undertaken by the UK-based National Institute for Health and Care Excellence (NICE), drawing on the evidence submission made by manufacturers, the independent report of the Evidence Review Group and the final guidance issued by the Appraisal Committee. She is now developing methods by which to test a series of hypotheses regarding the use and acceptability of real-world data in these appraisals.

Ana Beatriz Mateus D'Avó Luís has been working on her PhD project Essays on Economic Incentives and Implications of Biomarker Tests, with supervisors Tommy Staahl Gabrielsen and Julie Riise, and also assisted by former CCBIO Associate Investigator Jan Erik Askildsen (all at the University of Bergen). D'Avó Luís investigated challenges and successes at the scientific, regulatory, and economic levels, aiming to clarify the implications of some of these challenges and successes for the development and use of biomarker tests. She successfully defended her PhD thesis in early 2021.

Important results
Review of the use of companion biomarkers in the management of colorectal cancer found that they could save some costs, however any saving was not large enough to make targeted therapies cost-effective. Furthermore, the cost-effectiveness of biomarker-guided therapies was more likely to be driven by the characteristics of corresponding drugs rather than those of companion cancer biomarkers. Although, one interesting finding was how inadequately the impact of the performance characteristics of cancer biomarkers on cost-effectiveness has been studied.

Current challenges
One of the main current challenges is to develop the methods of technology appraisal to facilitate the production of robust estimates of cost-effectiveness around the time new products are launched.

Focus and research aims in the coming years
The foci of the health economics group in the next few years concern the value of different types of evidence when assessing cost-effectiveness and understanding how economics can better inform decision making over new health technologies. In both cases, the context is oncology treatments, with a particular emphasis on biomarkers and molecular targeted therapies. ••

GROUP MEMBERS:

Cairns, John, MA, MPhil, professor, associate investigator, group leader
Seo, Mikyung Kelly, MA, PhD candidate
Kang, Jiyeon PharmD, MS, PhD candidate
Gabrielsen, Tommy Staahl, MA, PhD, professor
Riise, Julie, MA, PhD, associate professor
Luís, Ana Beatriz Mateus D'Avó, MA, PhD candidate

BIOINFORMATICS AND BIG DATA

INGE JONASSEN

Research focus
The Jonassen group works 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. They are currently working on a system medicine approach utilizing machine learning approaches targeting leukemia and development of methods to exploit the Hyperion technology to the study of tumor-microenvironment interactions in solid cancers.

Subprojects
Jonassen leads the project AML_PM funded by ERAPerMed, including Bjørn Tore Gjertsen as a partner 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. In the fall of 2020, a new postdoc was recruited to work on development and use of methods to exploit the Hyperion imaging technology to the study of tumor-microenvironment interactions. Current work includes establishing pipelines and designing analysis approaches for data sets to be generated within CCBIO.

Important results
Relevant to Jonassen's work in CCBIO, he published (in IEEE BIBM) in 2019 a new framework or feature selection / biomarker identification integrating feature selection stability, and in 2020 he contributed to a deep learning approach integrating gene annotation, proteomics and gene expression data proposing a new method to extrapolate protein expression data. These approaches will be explored also in context of the mass cytometry and Hyperion data analyses undertaken in context of CCBIO where expression data is obtained for a relatively small set of proteins.

Current challenges
The Jonassen group aims to develop and use mathematical models that capture and predict effects of drugs targeting signaling molecules. Through the AML_PM project, 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.

Focus and research aims in the coming years
The new EraPerMed project is tightly linked with CCBIO and will be an important focus for the Jonassen group in the coming three years. In addition, 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
Ehsani, Rezvan, PhD, postdoc
Horsberg, Kristian Høy, master student
Kleftogiannis, Dimitrios, PhD, postdoc
Wimalarasan, Akilina, master student


4

STRATEGIC ADVICE

ROLF K. REED

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 under the CCBIO umbrella and is affiliated to the Lorens group at the Department of Biomedicine.

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 2020, 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. Also, he has continued in the Biosciences Panel of European Academies of Sciences Advisory Council as the representative for The Norwegian Academy of Science and Letters.

Reed has received numerous awards in his career, the most recent was October 14, 2020, when he was awarded with the prestigious Norwegian King's Medal of Merit, presented to him by the Mayor of Bergen. The medal is awarded to individuals as "a reward for efforts of a particularly socially beneficial nature in fields such as art, culture, science, business, social and humanitarian work."

Research activities

Reed's research activities are currently focused on a collaboration on PDX-models with Linda Stuhr. Another ongoing project is the turnover of potential biomarker proteins, such as AXL, 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 Jim Lorens and Olav Tenstad at the Department of Biomedicine. However, as most other research projects, these have been delayed due to the corona measures.

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International Faculty

The CCBIO International Faculty consists of internationally high-ranking scientists within relevant fields of cancer research. They have 10% adjunct professor or researcher positions at CCBIO, University of Bergen. The early establishment of such firm collaborative ties has increased CCBIO's ability to perform cutting-edge research by conducting joint projects, facilitating the transfer of knowledge, and by receiving high-level strategic advice and support. The faculty members have successfully strengthened CCBIO's collaborative networks. Another important aim has been to enable CCBIO's Research School to have research-based courses at the highest level and to enable co-supervision and exchange of PhD candidates and postdoctoral fellows. In 2020, CCBIO's International Faculty numbered 14 affiliated investigators, and CCBIO clearly feels that this unique group has strongly supported the center's many activities and efforts.

Frédéric Amant

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 during 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.

Marta Bertolaso

Marta Bertolaso is professor of Philosophy of Science at the Faculty of Science and Technology for Humans and the Environment at University Campus Bio-Medico of Rome, where she is the director of the Research Unit of Philosophy of Science and Human Development. She teaches Epistemology of the Experimental Design, Human Ecology & Sustainability, Digital Mindset Transitions for undergraduate and graduate students at the same university.

Her expertise in philosophy of life sciences and scientific practice, and philosophy of complex organized systems has allowed her to promote and collaborate in interdisciplinary research and educational projects. She is currently focusing her work on an integral understanding of organismic development and promoting an integral view of personalized medicine as Editor in Chief of the Springer Series on "Human Perspectives in Health Sciences and Technology". Marta Bertolaso is thus also developing a notion of human work, and organizations that might better match the current complex scenarios and the possibilities of technological advancements. She is currently contributing, in collaboration with companies and enterprises, to the development of ecosystems' accelerators for a renewed industrial and social development after the COVID-19 epidemic.

Her collaboration with CCBIO relies upon the work she did on cancer research and cancer biology in the last two decades, from which also the paradigm of integral development emerged. In particular, she is focusing on the assumptions and epistemological foundations for an adequate identification and implementation of biomarkers for cancer's diagnosis and treatment. She is currently discussing explanatory advantages and limits of different models of carcinogenesis, cancer development and heterogeneity with Lars A. Akslen and Roger Strand for a more comprehensive understanding of some empirical results the CCBIO teams are currently focusing on. She has also concluded an editorial project with other colleagues in the field, for MIT: "Rethinking Cancer, A New Paradigm for the Postgenomics Era", by Bernhard Strauss, Marta Bertolaso, Ingemar Ernberg and Mina J. Bissell.

Jean-Christophe Bourdon

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. His 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 the investigation of the p53 protein isoforms expression and activities in clinical samples (FFPE-IHC, flow-cytometry). These antibodies Dr. Bourdon has made available to the scientific community and pharmaceutical companies.

Dr. Bourdon has a long-lasting collaboration with Bjørn Tore Gjertsen on the development of the p53 isoforms as biomarkers in AML and breast cancer. They also co-supervise a PhD project (Ehsan Hajjar), 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). Hajjar has successfully completed his PhD and several publications are expected in 2021.

Dr. 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. He would also like to develop new diagnostic tools related to the p53 isoforms in partnership with CCBIO.

Rolf A. Brekken

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 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 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 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 Lars A. Akslen and Jim Lorens.

Hani Gabra

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 as emeritus chair and honorary NHS consultant in medical oncology at the Imperial College London.

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 CCBIO, particularly around translational and clinical research for AXL targeted therapy.

Ritva Heljasvaara

Ritva Heljasvaara received her PhD in 1996 in biochemistry and molecular biology at the University of Oulu, Finland. After her postdoctoral training at the National Center of Biotechnology, Spain, in 1997-1998, she has been working in one of the world's leading extracellular matrix (ECM) and collagen research groups at the Faculty of Biochemistry and Molecular Medicine, University of Oulu, with the exception of a sabbatical in 2006-2007 at the University of Oviedo, Spain, for farther training in tumor biology. Since 2014, Dr. Heljasvaara has directed the collagen research group together with Professor Taina Pihlajaniemi, and since 2020 she has also directed the ECM-Hypoxia Research Unit, consisting of five internationally strong research groups which perform globally recognized research on ECM, fibrosis, hypoxia and vascular biology.

Dr. Heljasvaara is recognized for her expertise in collagen and tumor biology and for her work on experimental mouse models. Her current research focuses on understanding the functions and translational potential of collagens in skin, breast and lung cancers as well as in hematologic malignancies. The ongoing projects pursue, for example, the roles on basement membrane and transmembrane collagens in breast and skin cancers and tissue and cancer stem cells, and the crosstalk between the cancer cells and osteoblasts in acute myeloid leukemia. In collaboration with Donald Gullberg, Dr. Heljasvaara is using mouse models to investigate the role of the fibroblast-specific integrin α11 in solid cancers, especially in cutaneous squamous cell carcinoma (cSCC). The key findings show that α11 is upregulated in cSCC stroma in human and mouse, and that it has a supportive role in skin tumorigenesis with effects on carcinoma-associated fibroblast differentiation and ECM organization.

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, Deputy Director of the Center for Cancer and Aging, and Dean of Postdoctoral Training at the Beckman Research Institute at City of Hope National Cancer Center, California.

Professor LaBarge's principal 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 make women more susceptible to cancer initiation. 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 long-term 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. This collaboration continues to explore the role of cytokeratins in aging and cancer susceptibility. 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.

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 and Deputy Head of the Nuffield Department of Surgical Sciences at the University of Oxford. In addition, he is an alumni 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. The biological focus of his work is on the interplay between metabolism and epigenetics in the development of treatment-resistant cancer. This work is support by interdisciplinary research teams led by computational biologists, surgical clinician scientists and pathologists through collaborations in the US and Europe. A number of these collaborations are in Norway and several former group members are now establishing independent academic careers there as well as in other Nordic countries.

Over the course of the last year there have been a number of collaborative biomarker and risk stratification papers arising from this work that align to the mission of CCBIO. Mills and collaborators have published the multi-cohort validation of a blood-based protein biomarker, LRG1, which stratifies patients based on progression risk at diagnosis and also for treatment with radiotherapy and androgen deprivation therapy. They have also published a cost-effective and robust methodology for the collection of urine samples at-home to support biomarker testing. Finally, they have further refined polygenic hazard models and genetic risk scores to identify subgroups who may benefit from more frequent imaging and/or PSA testing, and also started to refine these scores to account for variations in genetic risk associated with ethnicity.

Klaus Pantel

Klaus 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.

Professor 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 105. 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 European Liquid Biopsy Society (ELBS, 2019-present) 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 (e.g., ISMRC Conference, October 2020), he has organized a unique infrastructure with large patient cohorts at the Comprehensive Cancer Center Hamburg (UCCH) of 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 CCBIO, Professor Pantel has a broad collaboration with CCBIO's researchers, 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. A joint manuscript is currently under review. Professor Pantel was also co-organizer of the CCBIO Satellite Symposium on Liquid Biopsies which took place the day before the CCBIO Annual Symposium, May 22nd, 2018 at Solstrand outside of Bergen.

Therese Sørlie

Therese Sørlie got her PhD at the University of Oslo in 2000. She is currently head of the Department of Cancer Genetics, Institute for Cancer Research at Oslo University Hospital and adjunct professor at the University of Oslo, Medical Faculty. Sørlie's group investigates breast tumor initiation and progression, with a particular focus on the cellular origins of breast tumors and further development into the intrinsic molecular breast tumor subtypes. The aim is to develop biomarker profiles that can predict the potential aggressiveness of early breast cancer and contribute towards reducing overtreatment for breast cancer patients.

The collaboration with CCBIO and Lars A. Akslen is rooted in 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.

Arne Östman

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 acted as coordinator for the Swedish Research Council-supported STARGET center-of-excellence 2006-16. Since 2020 he is a member of the Nobel Assembly.

As Professor II at CCBIO since 2015, Östman has obtained two rounds of funding from the Norwegian Cancer Society (NCS), 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 with the NCS-funded staff located at CCBIO. This project is presently being expanded to also involve researchers at Uppsala University and the FIMM institute in Helsinki. A key asset for these studies is CCBIO's Hyperion Imaging System.

In 2016, Östman, together with Akslen, co-organized the first Scandinavian Pathology Seminar (SCANPATH) at Sotra, gathering Scandinavian tumor pathologists. The initiative has since been followed by annual SCANPATH meetings 2017-19 and will be continued with a 2021 meeting in the southern part of Sweden. Östman also took part in a former EU grant application together with Donald Gullberg, contributed with one chapter to the recent collection of reviews on tumor microenvironment edited by Akslen and Watnick, and has committed to a chapter for a planned 2021 second edition.

Jean Paul Thiery

Jean Paul Thiery is currently senior research fellow at the Guangzhou Regenerative Medicine and Health, Guangdong Laboratory. He held the position of Director of Research at Centre National de la Recherche Scientifique (CNRS), Paris. Later, from 1995 to 2003, he established and headed the Cell Biology Department of the Institut Curie. He was the inaugural Director of the Department of Translational Research at the Institut Curie Medical Division. In October 2006, he moved to Singapore where he was Deputy Director of the Systems Biology Division at the Institute of Molecular Cell Biology until November 2011 and Chief Scientific Officer of the Experimental Therapeutics Centre of A*STAR until April 2011. He was then appointed Professor and Head of the Department of Biochemistry of the Yong Loo Lin School of Medicine at the National University of Singapore (NUS). Concurrently he holds a Research Director position at IMCB A*STAR, a senior Principal Investigator position at the Cancer Science Institute and a position as an Associate Principal Investigator at the Mechanobiology Institute (MBI) at NUS. Since July 2015, Jean Paul Thiery is Emeritus Research Director at the CNRS research unit "Matter and Complex Systems" in Paris. He also holds a Research Director Emeritus position at the Institut Gustave Roussy in Villejuif, the largest Comprehensive Cancer Center in Europe. Jean Paul Thiery has been a Toh Chin Chye Visiting Professor at the School of Medicine at NUS. He is a visiting professor at the Li Ka Shing faculty of Medicine of Hong Kong University.

Professor Thiery has made seminal contributions in the fields of cell adhesion, cell migration, morphogenesis, and cancer, publishing more than 490 peer-reviewed articles in different areas of the life sciences (h-index above 110). In 1977, together with Prof. Gerald Edelman, Nobel Laureate in Medicine, he discovered the first cell-cell adhesion molecule: N-CAM. He has pioneered new physical approaches to measure the strength of intercellular adhesion in epithelial cells. He has shown the critical role of actin microfilament dynamics in adhesion strengthening and of alpha catenin in mechanosensing and has contributed to revisit the origin of the mesectoderm, with findings that suggest the mesectodern and the neural crest come from two distinct territories in the ectoderm.

Jean Paul Thiery characterized a murine mammary stem cell, which can lead to basal-like tumors upon integration of a truncated β-catenin. More recently, he was able to identify a new set of breast cancer genes based on transposon insertional mutagenesis. Professor Thiery co-discovered important activating point mutations in FGFR3 in bladder carcinoma, now considered the best prognostic marker for superficial tumors. He has also obtained gene expression and gene alteration signatures for breast carcinoma, ovarian carcinoma, bladder carcinoma

and uveal melanoma to define new prognostic indicators. Jean Paul Thiery has established a diagnostic (Dx) kit for the detection of bladder cancer. He is also considered the first to propose that epithelial-mesenchymal transition (EMT) is a crucial mechanism for the progression of carcinoma. He has established a high-throughput screen for EMT in carcinoma to define drug combinations that circumvent resistance to therapy.

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.

Randolph Watnick

Randy 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 (VBP) 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. Dr. Watnick has also since 2017 been coordinating the VBP's part of the CCBIO-INTPART program, engaging actively in teaching at CCBIO courses and at the Scientific Writing & Communication Seminar. ••

Research School for Cancer Studies: Courses at CCBIO

The CCBIO Research School for Cancer Studies (RSCS) focuses on educational activities related to translational cancer research and innovation, including international exchange and mobility. Ethical, legal and societal aspects of cancer research and treatment are also focused upon. The RSCS has in the last two years expanded its activities considerably under the leadership of Elisabeth Wik. RSCS courses are available for all researchers, PhD candidates and master-level students, also outside of CCBIO. Participants can opt to receive ECTS or attend for the transfer of knowledge only. All events are announced also outside of CCBIO, through a Nordic portal, and by help of CCBIO's international faculty and networks.

The 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 its strategic activities, like the CCBIO Annual Symposium, CCBIO Junior Scientist Symposia and CCBIO Research Seminars, into the RSCS. Due to the pandemic, the CCBIO Annual Symposium could not be arranged in 2020, but after a short period of adaptation to digital formats, all other activities were performed digitally from May onwards.

When inviting speakers for lectures and seminars, CCBIO normally uses the opportunity for both young and senior researchers to have targeted meetings where potential points of common interests are mapped out. In combination with the recruitment of an international network of international affiliated researchers, this ensures that the center's younger researchers have access to renowned national and international scientists from other research communities.

As the pandemic forced CCBIO and the RSCS to run seminars and courses online, the scope for networking became somewhat restricted. On the positive side, making RSCS activities available online has enabled CCBIO's extended international network to take part. In particular, PhD candidates and postdocs from collaborating Nordic universities took advantage of this, with up to 300 participants on a single RSCS course. This has given CCBIO's young researchers the possibility to engage in group discussions and assignments with a wider range of international colleagues. The course organizers were a bit apprehensive of the students' feedback, as the planning and execution of the initial online versions had to be done rather quickly. Nevertheless, the reviews confirmed the standard of the courses as befitting a Center of Excellence. Interestingly, a majority of the participants reported that online courses suited them perfectly, and that they would prefer future CCBIO courses to be online, also after the pandemic. However, CCBIO and the RSCS see on-site networking during courses as being of great value, and will consider running future courses as hybrids, allowing for both on-site and online participation.

The RSCS is very grateful for the assistance provided by the University of Bergen's IT department and the Læringslab for swiftly setting up courses online and providing support and training. CCBIO is also very grateful to the Department of Clinical Medicine's Kjetil Harkestad and several staff at the Faculty of Medicine for their flexible administrative support towards the RSCS.

In 2020, CCBIO held the courses that run continuously (CCBIO901 and -902), as well as CCBIO903, -905, -906, -907 and -908. Six of these courses mainly took place after the onset of the pandemic and were held online. You can read more about these activities in separate paragraphs. For 2021, the RSCS plans to run CCBIO901 and -902 continuously as well as -908 (April), -903 (May-June), and BMED904 (June), as well as launching a number of new ECTS awarding courses.

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 annually, 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

CCBIO903 is a two-week, 5 ECTS PhD course designed as a unique opportunity for PhD candidates to question the assumptions underlying their work, reflect on and discuss the robustness of their research, and anchor it in broader ethical, legal, social, economic, and political contexts. The core of the course is structured around the book volume edited by Anne Bremer and Roger Strand: *Cancer Biomarkers: Ethics, Economics and Society* (2017), and aims to address several key questions:

1. What are the promises, limitations, and consequences of the "imaginary" of precision cancer medicine?

2. 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?

3. How do we take medical decisions when faced with risks, uncertainties and even ignorance?

4. In a highly medicalized culture, what does a "good life" look like for (future) cancer patients?

5. What are the patient's perspectives on oncology research, treatment, and news coverage?

6. How is precision oncology addressed in the media? What consequences does this have on society, politics, and science?

7. What is fair priority-setting for distributing the newest precision cancer therapies?

8. 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:

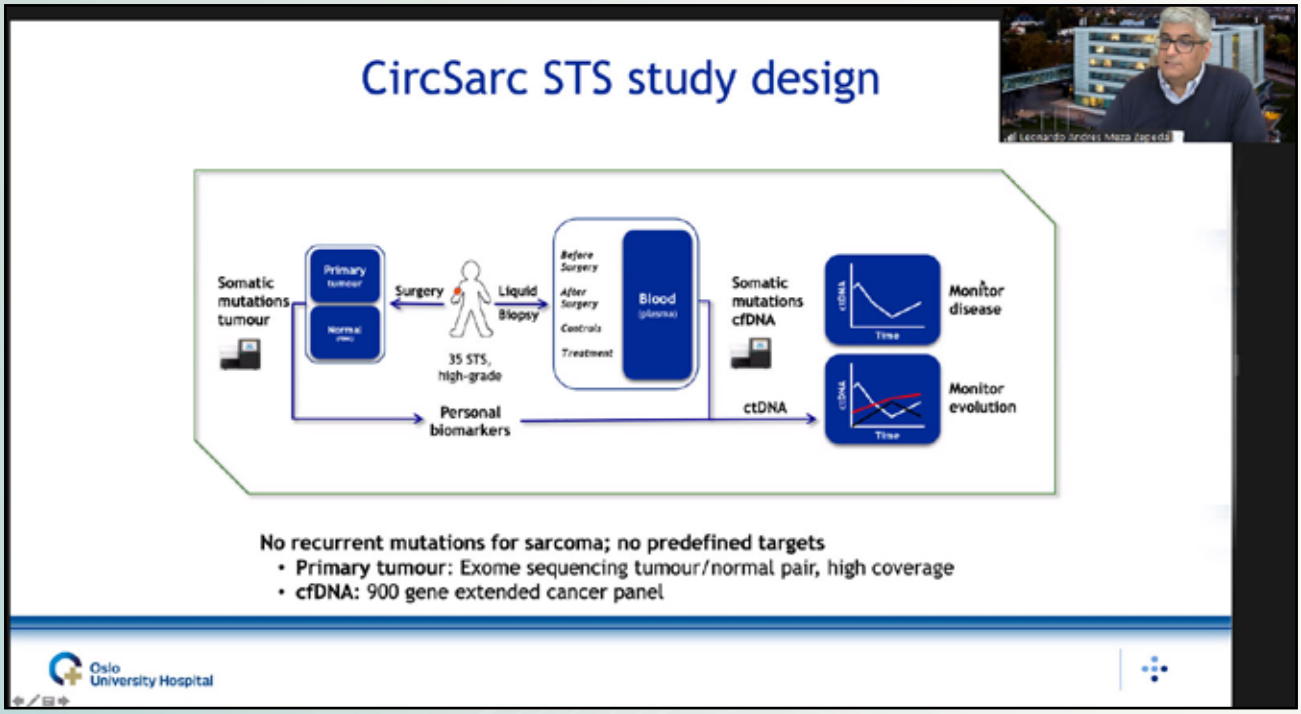
- **The course is highly interactive, and the lectures invite the participants to take part in extended reflexive discussions with the teaching team and among themselves. At the end of the course, all candidates are asked to present their research in relation to broader social, ethical and/or economic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

- **The teaching team is highly interdisciplinary (Roger Strand from philosophy of science, Anne Bremer from science and technology studies, and John Cairns from health economics). In addition, several guest lecturers are invited to share their perspectives across disciplines ranging from oncology, philosophy of medicine, media studies and prioritization of health care.**

- **The course generally concludes with a special seminar, open to all, with an expert panel discussing a specific cancer related issue in depth. In January 2020, the special seminar was on "Cancer in the news", with presentations from Mille Stenmark and Irmelin Nilsen from the Centre for the Study of the Sciences and the Humanities, and extensive discussions with panelists Tine Dommerud, Aftenposten and Knut Helland, the Department of Information Science and Media Studies.**

The course has been held five times since 2015, and while initially targeted for CCBIO's PhD candidates, it has in the last years been made available to cancer researchers and PhD candidates nationally and internationally. In 2020, the second week of CCBIO903 was held in January, following the first week in December 2019. 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 from several geographical locations, such as Bergen, Oslo, Finland, London and Boston.

CCBIO903 is co-organized and taught by three members of the ELSA and Economics groups in CCBIO: Roger Strand, Anne Bremer and John Cairns. The course will next be held during two weeks in June and September 2021 and will include sessions based on the upcoming second volume edited by Anne Bremer and Roger Strand: *Precision Oncology and Cancer Biomarkers: Issues at Stake and Matters of Concern* (upcoming, Springer Series Human Perspectives in Health Sciences and Technology).



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 and morbidity. The course has particular focus on 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, aiming to give PhD candidates in cancer research a broad understanding of various aspects of tumor biology based on updated knowledge. The PhD candidates will also gain deeper insight into how knowledge about tumor biological changes affects our strategies to customize assessment and treatment for this group of patients.

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 by a one hour written exam.

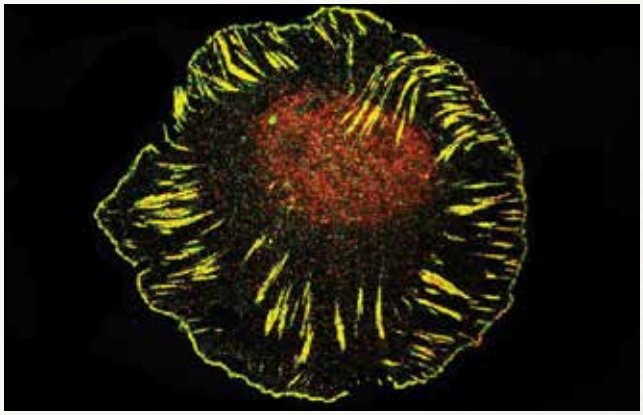
In 2020, the course was postponed from April to May 25-27, giving time to adapt CCBIO904 into CCBIO's first digital course. This was also CCBIO's first experience with an unexpected high level of interest in digital courses from national and international participants, a tendency holding true also for later courses. Having only 60 spaces in the planned format, registration had to close early. Participants came from the other Nordic countries, elsewhere in Europe and even from California.

The organizers, with no prior experience and little training in holding courses online, had to manage different lecturers and the 60 participant's group work and assignments in Zoom. But all went well and Zoom turned out to be an excellent teaching tool. Most of the talks were given live and some were uploaded as Kaltura Videos. The experiences from CCBIO904 proved to be of significant value for planning the remainder of CCBIO's courses in 2020.

Oddbjørn Straume has the academic responsibility and Reidun Kopperud is the course coordinator. The next course will be in spring 2022.

BMED904 – Matrix Biology

BMED904 is a well-established 3 ECTS 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. The course runs over five days every second year and includes lectures from local researchers and several internationally well-known scientists within the field of matrix biology. Practical laboratory training is also included.



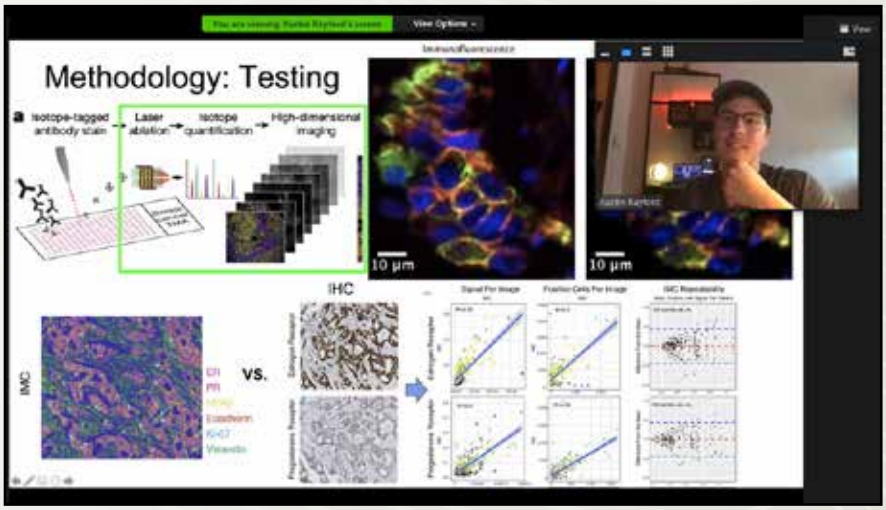
The course focuses on basic molecular mechanisms pertaining to the biological role of the extracellular matrix. The last course was last held in June 2019, with fourteen participants. Attending students were from Bergen, other cities in Norway and from Finland. Three lecture highlights included John Couchman (Copenhagen), Cathy Merry (Manchester, UK) and Joanna Philips (UCSF, San Francisco). In addition to attending lectures, the students read relevant articles, worked on articles group-wise and presented their articles for the rest of the group. All students also spent time in the Matrix Biology Lab, where microscopy of integrin-tagged cells as well as cell cultures in 3D collagen matrices were demonstrated. The participating students evaluated BMED904 as excellent and well organized, with inspiring and interesting lectures giving a good overview of the ECM and its importance in heath and disease.

The next course will be in June 2021, covering 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. A new theme, the role of cancer associated fibroblasts in cancer and ECM, will also be covered. In addition to local experts, lecturers include a range of international experts in the field. In 2021 the course will be combined with a DIKU summer school in fibrosis that is part of the MOTIF-network (https://www.uib.no/motif/141491/diku-summer-school-fibrosis-2021). Due to the uncertainty caused by the pandemic, the course is planned to combine face-to-face "seat time" for students attending in Bergen with online presentations of all lectures and lab demonstrations. The lectures are open to all interested.

BMED904 is organized and executed by Marion Kusche-Gullberg and Donald Gullberg.

CCBIO905 – Methods in Cancer Biomarker Research

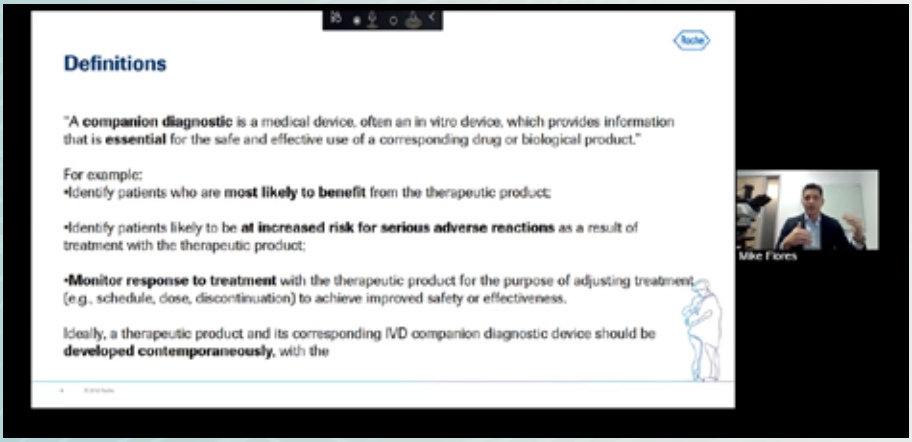
CCBIO905 is a 5 ECTS PhD-level course focusing on the full panel of advanced and standard methods with relevance for cancer biomarkers. The thematic parts cover a wide range of methods, from basic techniques on nucleotides and proteins to advanced single cell high-dimensional approaches, as well as bioinformatics and bio-banking. The course was established in 2015 and was run digitally for the first time October 27-29, 2020. Registration was split between students wanting ECTS and those interested in professional updates only. This made it easier to organize mandatory attendance to digital group assignments for the former group. The course was well attended with 80 participants following lectures and 34 students completing the full course to earn ECTS. The participants came from 15 different universities and 8 different countries, with the majority of students from Norway and Finland.



The participants learnt how various biological specimens (tissue samples, blood samples, urine samples, and other

biologic materials), may be studied by a variety of methods, and how to analyze the results by bioinformatic tools. The 2020 course noticed an increased focus on advanced *in vitro* models, including organoid cultures, and a thorough theoretical introduction to high-dimensional single cell analyses using flow mass cytometry and imaging mass cytometry (IMC). CCBIO's Hyperion Imaging System has been available to researchers in Norway since 2019, and several student presentations also covered this exciting novel technology. Dr. Mike Flores from Roche Diagnostics gave an interesting talk about companion diagnostics; medical devices providing information that is essential for the safe and efficient use of a corresponding drug or biological product, explaining the clinical needs and current research and development in the field.

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 group presentations were given an insightful evaluation by an expert panel consisting of Jim Lorens, Liv Cecilie Vestrheim Thomsen and Cornelia Schuster. The course was concluded by a two-hour multiple-choice examination.



Lars A. Akslen and Agnete Engelsen have the academic responsibility and Ingeborg Winge is the course coordinator. The next course will be in the spring term of 2022.

CCBIO906 – Cancer Genomics

CCBIO906 is a 3 ECTS course providing a broad understanding of aspects in cancer genome biology and investigations 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 of 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 2017. In 2020, the course was held February 20-21, with 40 students enlisted, in large part local, but also from Oslo, Sweden, Denmark, Austria, Finland and even from Tanzania. This was before the pandemic situation, with on-site participation only.

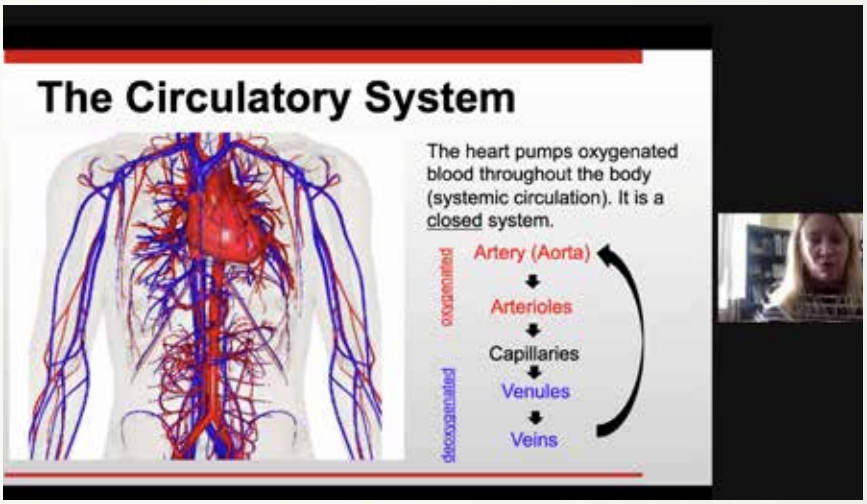
Ola Myklebost has the academic responsibility, and Rebecca Nguyen is the course coordinator. The next course will run in the spring term of 2022.

CCBIO907 – Cancer-Related Vascular Biology

CCBIO907 is a two-week intensive course (6 ECTS) that is part of the CCBIO-Harvard INTPART collaboration, aiming to provide 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. Topics range from discovery to clinical application, lymph-angiogenesis and vascular biology in non-cancerous diseases. 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 covered. The course aims to stimulate scientific thinking and professional discussions. Participants benefit from experienced lecturers from the Vascular Biology Program at Boston Children's Hospital and Harvard Medical School who have been in the frontline of vascular biology research for decades.

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 the assignments, the students present project ideas, ranging

from hypotheses to suggestions on experimental design, including funding proposals. This year, important soft skills themes were also presented, like "Crafting your pitch" (Diane Bielenberg), "Crafting a presentation" (Bruce Zetter), and "Fundamentals of Peer Review" (Joyce Bischoff).



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 in 2018. Due to the pandemic, the 2020 course was held online September 21 to October 2 and on October 9. Digital participation boosted attendance, and 96 students and researchers took part, their affiliation ranging from Bergen to all over Norway, Finland, Sweden and Denmark, as well as a number of other countries. Digital implementation made it practicable to interact with a much larger group of participants in a satisfactory manner. The organizers capitalized on the multinational nature of the assembly by making sure to organize group work so as to facilitate international networking.

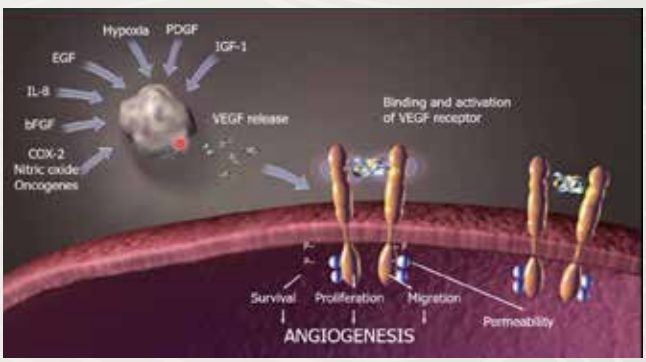
Michael S. Rogers from the Vascular Biology Program (VBP) contributed in an excellent manner with program planning and facilitated the US collaboration for this course. VBP faculty contributing with lectures this year included Bruce R. Zetter, Michael S. Rogers, Joyce Bischoff, Edward Smith, Hong Chen, Diane R. Bielenberg, and Randy S. Watnick, in addition to CCBIO's local experts Reidunn Edelmann and Oddbjørn Straume. Selected international lectures were open to a broader audience through four CCBIO Seminars and Special Seminars.

Elisabeth Wik and Lars A. Akslen have the academic responsibility, and Heidrun Vethe is the course coordinator. The next course will run in the fall term of 2022.

CCBIO908 – Scientific Writing and Communication Seminar

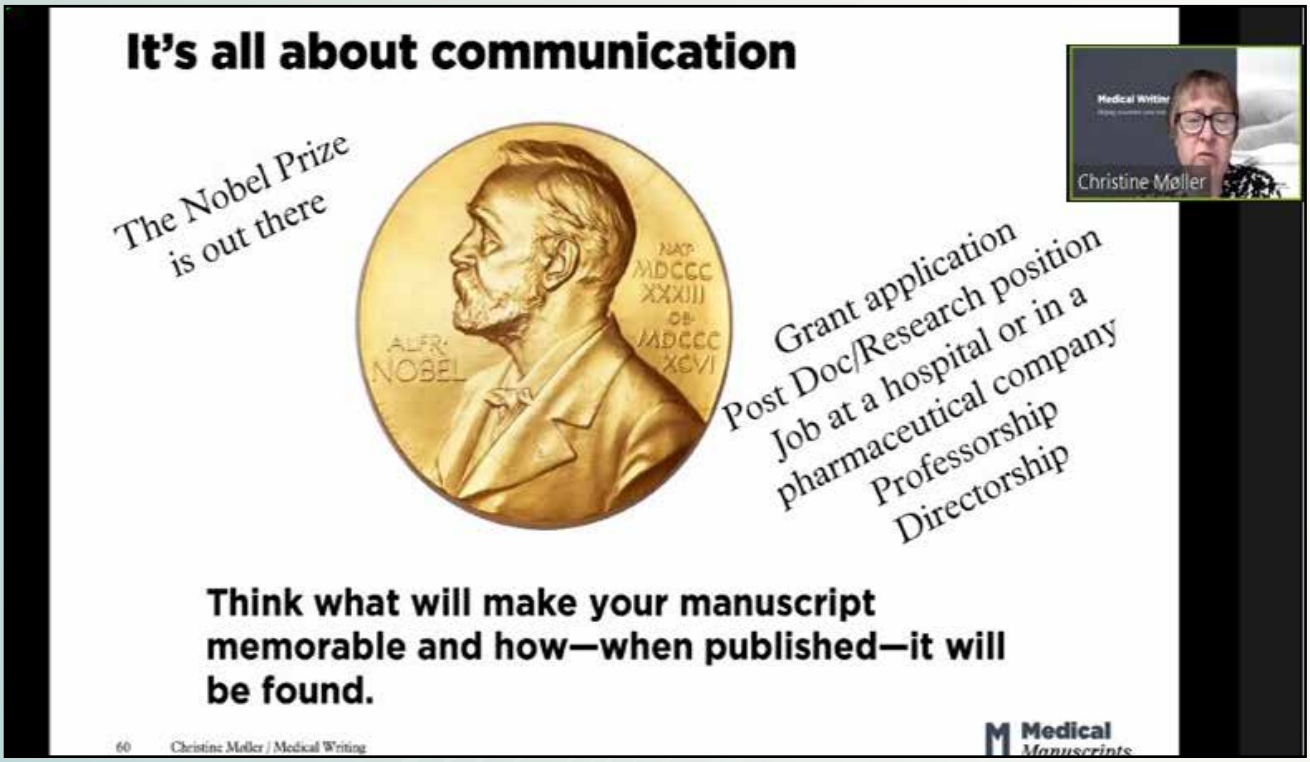
CCBIO908 is a newly approved 2 ECTS adaptation of a non-credit-giving course that has been part of the CCBIO-Harvard INTPART collaboration since 2017. It covers topics such as organizing ideas, improving manuscripts, clear writing, scientific storytelling, titles and abstracts, cover letter, common mistakes and making a manuscript memorable.

CCBIO908 was the second CCBIO course held online and the level of interest came as somewhat of a surprise. At close to 300 participants, attendance was overwhelming the Faculty of Medicine's ability to register participants for ECTS. Hence, registration had to be closed even though the course format could have held a higher number of participants online.



In addition to local and Norwegian participants, 150 students from institutions in Finland, Sweden, Iceland and Denmark attended. This level of attendance would not have been possible in the traditional format. The Zoom breakout rooms were great for letting the students meet in smaller groups to discuss their assignments and texts before the plenary discussions.

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 from the Vascular Biology Program and Harvard Medical School. In addition, CCBIO's media advisor Marion Solheim contributed with a recorded session on science presentation, showing how to make a presentation stick – in a good way, also covering the use of language, layout and how to avoid information overload, as well as body language and tone of voice.

In 2020, CCBIO908 was held on June 8 and 11. The next course will be on April 12 and 15, 2021, also this time online. Registration will be split with separate registration for students wanting ECTS.

CCBIO's academic responsible in 2020 was Elisabeth Wik, with Vandana Ardawatia as coordinator. In 2021, CCBIO's research advisor Yamila Torres Cleuren will share the academic responsible with Elisabeth Wik.

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-Harvard INTPART collaboration. CCBIO students at master and PhD levels have since been offered a summer internship at VBP labs. In 2018 and 2019, three students attended this program each year for 8-12 weeks. PhD candidates as well as 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. 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 all reported that they were warmly welcomed by the PIs and other colleagues at the host labs. By participating in lab meetings, observing presentations, and receiving feedback, they were stimulated to be curious and ask questions, and they observed how critical discussions brought the scientific work forward.

In CCBIO's view, to be part of more than one top-notch scientific environment is an important impetus for up-and-coming researchers "to pursue ideas and ambitions and excel your own standards" (as stated by Bruce R. Zetter in 2018, at the CCBIO seminar entitled "What is Scientific Excellence"). Joining the Lab Visit Program has proven educational, challenging, and inspiring, and all CCBIO students attending have reported great educational and scientific benefits from their summer in Boston. Networking with students and faculty at the VBP is rewarding for the students, and of great value for their research careers.

Lab visits were planned for 2020 but were postponed due to the pandemic. The program will be resumed when possible. If pandemic-related travel restrictions are still in place in summer 2021, possibilities for "digital lab visits" will be explored.

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 interventions to be tested in humans.

Clinical trials are studies performed in humans, aimed at evaluating one or more medical, surgical or behavioral intervention. Such trials are 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 increasingly used. 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 survival and prevention of recurrence.

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

The course modules are based on the ICH GCP, and the participants received a certificate in Good Clinical Practice on completion of the course. As part of the collaborative effort with Neuro-SysMed (see below), this course will be expanded and run in the fall term of 2021 as an ECTS rewarding course.

Currently Line Bjørge and Hani Gabra (CCBIO international faculty) have the academic responsibility and Reidun Kopperud is the course coordinator. For the future ECTS-rewarding course, Line Bjørge and Øyvind Grytten Torkildsen (Neuro-SysMed) will have joint academic responsibility.

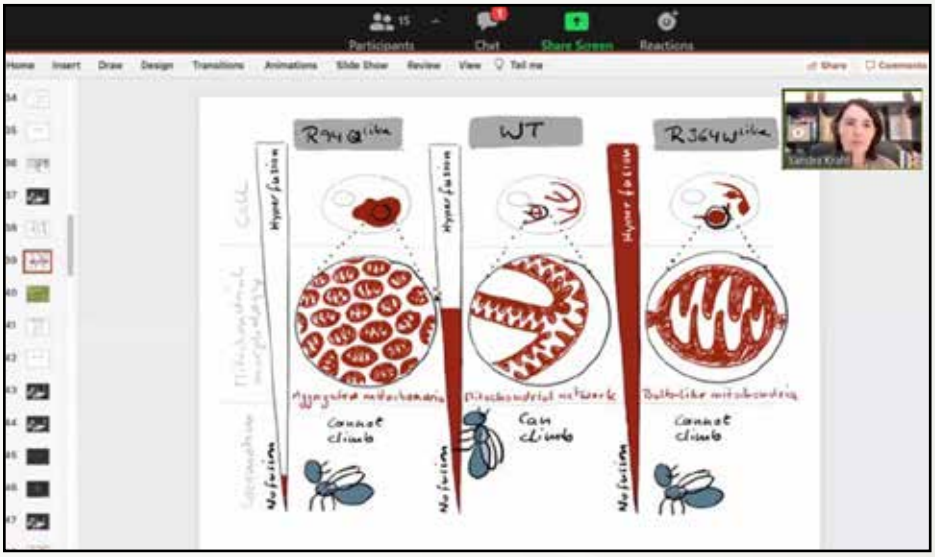
Workshop: Applying Design Principles to Schematic Figures (EMBO-CCBIO)
December 8 and 9, 2020, CCBIO joined forces with EMBO for the workshop Applying Design Principles to Schematic Figures, as part of the CCBIO INTPART program. 13 selected participants attended. EMBO is an organization that aims to support researchers around the world at all career stages, to stimulate the exchange of scientific information and to provide help to advance young scientists research, by teaching professional and "soft skills" that are critical for a successful career in science.

The workshop is developed by freelance graphic designer Sandra Krahl. She gave the participants important input on how to design illustrations in scientific publications and other media channels, in order to communicate research findings and drawing attention to scientific work. Starting off with a "draw-my-life", she walked the participants through the important elements of storytelling, fonts, colors and how elements with correct highlight and sizes can turn simple sketches into professional and precise figures. Krahl made clear how drawings are a simple, yet powerful, tool of communication and introduced a multitude of tips and tricks that will be helpful alongside writing one's own scientific work. The participants were then able to try for themselves through several interactive assignments. Their evaluations stated that such training is highly recommend for all scientists who wish to convey their findings in a striking and noticeable manner.

The workshop was facilitated by INTPART coordinators Elisabeth Wik and Randy Watnick, and CCBIO aims to run the workshop several times for young CCBIO researchers at regular intervals.

International Collaboration and Further Development of Courses
CCBIO has strong strategic emphasis on internationalization. As part of this effort, the center has recruited an international network of adjunct researchers that take an active part in projects and with tutoring of younger researchers, as well as in CCBIO RSCS courses, seminars and larger meetings. Other external international and national faculty are also invited as lecturers to courses and seminars. In total, this provides ample opportunities for CCBIO's own, as well as other students and researchers, to meet and interact with influential experts in the cancer research field. Following the first lockdown in March 2020, most in-person meetings were replaced by online activities. These changes have been an eyeopener towards venues for collaborative and mentoring interaction that will be further explored and exploited inn 2021, also after vaccination and the re-introduction of on-site meetings.

As part of CCBIO's internationalization effort, a project under the RCN and DIKU funded program for International Partnerships for Excellent Education and Research (INTPART) has been running since 2017. The basis for the project is a reinforcement of existing collaborations between



CCBIO and the Vascular Biology Program (VBP) at Boston Children's Hospital and 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 courses, CCBIO has established the new INTPART courses CCBIO907 Cancer-Related Vascular Biology and CCBIO908 Scientific Writing & Communication, the workshop on design principles with EMBO, the Boston Lab Visit Program and several seminars and other meetings, as well as integrating INTPART with CCBIO's existing activities.

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

• Local students attending the Scientific Writing & Communication 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 has been well received by the students, with an increasing number of attendees at the second course in 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 also attended this activity. The students attending have reported great educational and scientific benefit from their Boston stay. If pandemic-related travel restrictions are still in place in summer 2021, possibilities for "digital lab visits" will be explored.

• 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. When travel restrictions are lifted both in Norway and the US, CCBIO aims to set up a second CCBIO-VBP Research Meeting.

• The workshop Applying Design Principles to Schematic Figures was timely and well received by the participants, strengthening skills important for improved visualization of research data. It will be re-run for new batches of young researchers.

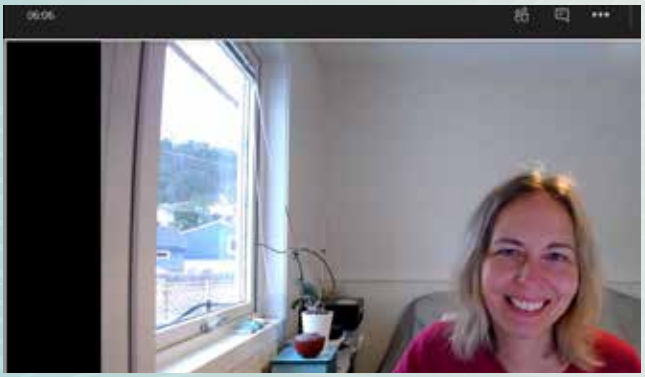
Lars A. Akslen and Marsha A. Moses (Director, VBP) are the INTPART project leaders, Elisabeth Wik is the main coordinator in Bergen and Randy Watnick the coordinator in Boston. For CCBIO907 and the CCBIO-VBP Research Meeting at Iceland in 2019, Michael Rogers was the VBP coordinator. In 2020, CCBIO was awarded an extended three years of funding for a second phase of the INTPART project (2021–2024), aiming to continue, consolidate, and further expand on the activities successfully established during the first INTPART project.

The CCBIO RSCS aims to continue and further develop the established courses (CCBIO901–908) and other activities together with its many excellent partners. Recently, CCBIO and Neuro-SysMed, a newly established RCN funded Centre for Clinical Treatment Research (FKB), has established a joint effort on new courses. As part of this, the partners aim to launch four ECTS-rewarding courses in 2021, on clinical trials, innovation in research, user participation in research and imaging mass cytometry. Neuro-SysMed and CCBIO will have joint academic responsibility for the courses that will be part of both centers' research schools. ••

CCBIO
RESEARCH SCHOOL
FOR CANCER STUDIES

Junior Scientist Symposium

The CCBIO Junior Scientist Symposium (JUSS) takes place four times a year and is part of the CCBIO Research School as the course CCBIO901. Junior scientists are invited to present their research in an academic environment, thus providing the opportunity for feedback across disciplines. The symposium acts as a practicing arena for presenters and participants as it allows them to communicate their own results and stimulate discussions. In addition, each meeting includes an inspirational lecture given by a more senior



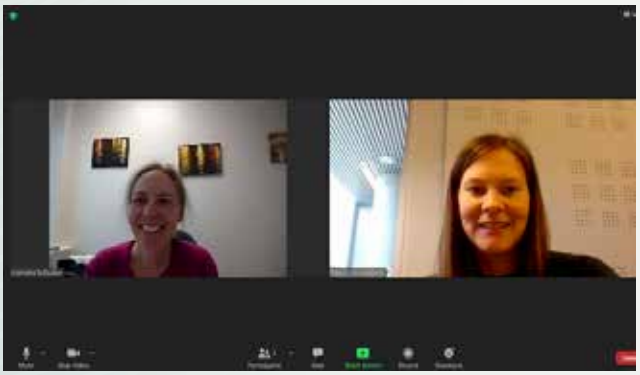
person, often someone from a different field of expertise. Students, PhD candidates, postdoctoral fellows, researchers, CCBIO faculty, staff and visitors are all welcome to attend the Junior Scientist Symposia.

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 encouraged to reflect on their projects and critically evaluate ethical aspects in their daily work. CCBIO901 provides 3 ECTS for students who give one oral presentation based on their own work, actively participate in at least 4 symposia, and write a three pages long scientific summary report based on four presentations.

During 2020, CCBIO held three symposia as the meeting scheduled for April was cancelled due to the recent COVID-19 lockdown. The remaining two symposia in 2020 were moved to digital platforms. Around 20 participants attended each of the two digital JUSS Zoom meetings in the fall of 2020. Online symposia proved to be much preferrable to cancelling, and the participants provided positive evaluations. However, the JUSS chairs clearly missed the possibility to meet and mingle with presenters and participants as this is an important part of the JUSS concept.

Each JUSS included presentations from PhD candidates, postdoctoral fellows and other researchers. Two of the inspirational keynote lectures were given by Yves Aubert and Yamila Cleuren, providing insights into planning innovative research and future careers. The symposia also included keynote lectures from Christine Stansberg (ELIXIR Norway) and Kari M. Ersland (Centre for Digital Life Norway), presenting possibilities for data analysis, collaboration and funding.

The organizers were happy to see that both presenters and audience adapted well to the digital solutions and contributed high-quality presentations and enthusiasm, thus maintaining the Junior Scientist Symposium as an encouraging and outstanding experience for both



participants and organizers. They nevertheless hope to be able to meet in person in 2021 to enjoy the discussions and possibilities for informal interaction and networking during breaks.

In 2020, the Junior Scientist Symposium was organized and chaired by Kenneth Finne, Cornelia Schuster and Maria Lotsberg. ••


Thermo

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
January 30, 2020
Conference room BBB

Symposium chairs:
Kenneth Finne and Cornelia Schuster

10:00–10:05 Organizers: Welcome

10:05–10:50 Keynote lecture:
Yves Aubert: "What is innovation, and how can my research become innovative?"

10:50–11:05 Break

11:05–11:25 Agathe Reigstad: "The pan-RAF and SFK inhibitor CCT196969 effectively inhibits melanoma brain metastasis *in vitro*"

11:25–11:45 Vandana Ardawatia: "Understanding the role of Nestin in basal-like breast cancer: Generation of a Nestin KO TNBC cell line by CRISPR/Cas9 editing"

11:45–12:30 Lunch

12:30–12:50 Reidunn Jetne Edelmann: "Analyzing tumor vessels with artificial intelligence"

12:50–13:10 Ida Herdlevær: "Investigating the Role of Microglia in Paraneoplastic Cerebellar Degeneration Using Imaging Mass Cytometry"

13:10–13:30 Austin Rayford: "Development and application of highly multiplexed imaging approaches in basic and translational AXL biology research"

13:30–13:35 Organizers: Wrap up and concluding remarks

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
September 17, 2020
Online event in Zoom

Symposium chairs:
Cornelia Schuster, Kenneth Finne and Maria Lie Lotsberg

09:00–09:15 Organizers: Welcome

09:15–10:00 Keynote lectures:
Christine Stansberg: "How may ELIXIR Norway help you analyze your data?"
Kari M. Ersland: "Centre for Digital Life Norway"

10:00–10:20 Break

10:20–10:40 Irene Matre Thowsen: "The role of skin lymphatics in salt-sensitive hypertension"

10:40–11:00 Jing Kang: "TAM receptor dynamics in melanoma therapy resistance"

11:00–11:30 Break

11:30–11:50 Anne-Maj Samuelsson: "Metabolomic signatures that predict heart failure in rats"

11:50–12:10 Anastasiia Rulina: "Role of obesity in development of breast cancer"

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
November 26, 2020

Online event in Zoom

Symposium chairs:
Cornelia Schuster and Maria Lie Lotsberg

09:00–09:10 Organizers: Welcome

09:10–09:55 Keynote lecture:
Yamila Cleuren: "Money and careers in science: where to start?"

09:55–10:15 Break

10:15–10:35 Madeleine Myrvold: "The prognostic value of MSI markers in endometrial cancer"

10:35–10:55 Trond Are Mannsåker: "The anti-tumor effect of cabozantinib on melanoma brain metastasis"

10:55–11:25 Break

11:25–11:45 Astrid Børretzen: "Epithelial-mesenchymal plasticity in aggressive prostate cancer"

11:45–12:05 Cecilie Askeland: "Differences in immune cell landscapes between hereditary and sporadic breast cancer"

12:05–12:15 Organizers: Closing remarks

CCBIO Masterclass Program

In 2020, CCBIO launched its own training program to help CCBIO's up-and-coming post-PhD researchers getting ready for their next career steps. Following a pilot seminar on Junior Application Writing (CCBIO-JAW) in late autumn 2020, the CCBIO Masterclass concept and program will consist of seven sessions during 2021, presenting different strategies and tools on how to perform efficient career planning towards independency for the young talents. The Masterclass program is coordinated by Yamila Torres Cleuren, in collaboration with CCBIO's director.

Each of the 10 selected participants, nominated as promising candidates from the various groups, will be paired with a scientific mentor from outside of their research teams, who will provide advice and help them navigate the difficult decisions that lie ahead. The Masterclass program will cover the following topics:

- **Mentoring and career development**
- **Conceptualizing research projects**
- **Research project management**
- **Establishing a research group**
- **Being a good leader**
- **Establishing research collaborations and networks**
- **Science communication**

In November 2020, the selected Masterclass candidates attended a two-day online seminar on Junior Application Writing (CCBIO-JAW), held by Yamila Torres Cleuren, and focusing on:

- **Identifying relevant opportunities**
- **Reading a grant call**
- **What should a good CV look like at different career stages**
- **How to write a good grant proposal**

The JAW participants were all very eager to learn more and had many questions on how to continue their careers. The participants' feedback was very positive, and the junior researchers applying for their first grants in 2021 will continue with group sessions to support their grant writing activities throughout the year.

Especially in the situation caused by the pandemic, there is an added layer of uncertainty, and this makes it particularly important to prepare the next generation of researchers for the challenges ahead. To this end, CCBIO will introduce the next Masterclass session in March 2021 as an online event. The final format of each session throughout 2021 will be subject to real-time changes in compliance with the COVID-19 regulations, emphasizing in-person attendance if possible. CCBIO looks forward to supporting the Masterclass participants' careers, expecting that they in turn will connect in collaborations and help each other throughout the years to come (see also CCBIO Opinion on Career Development).

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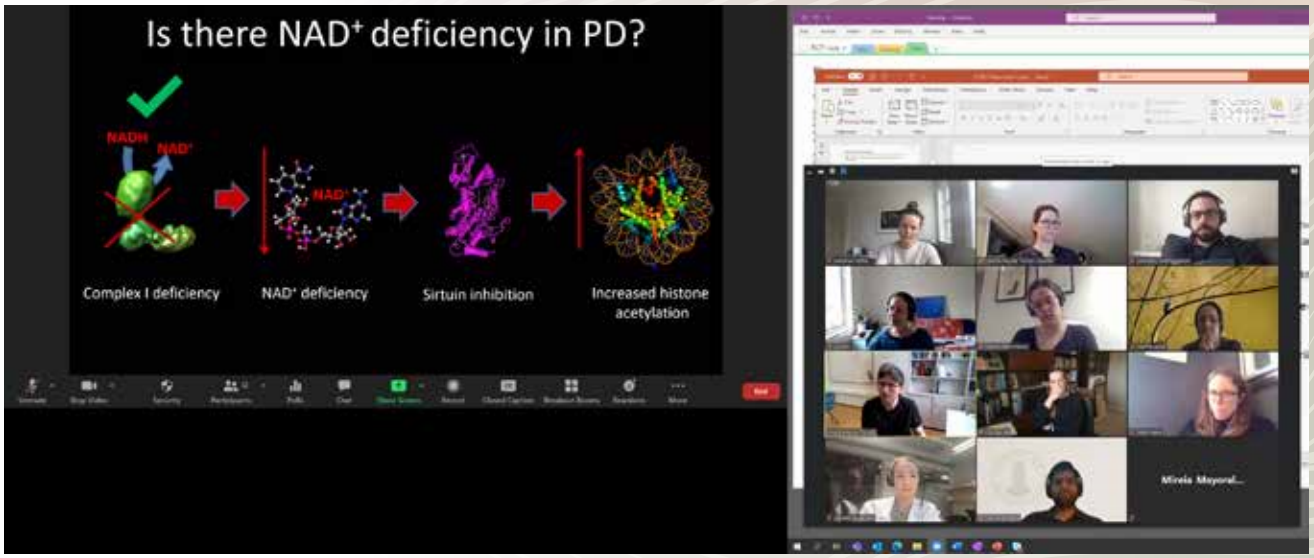
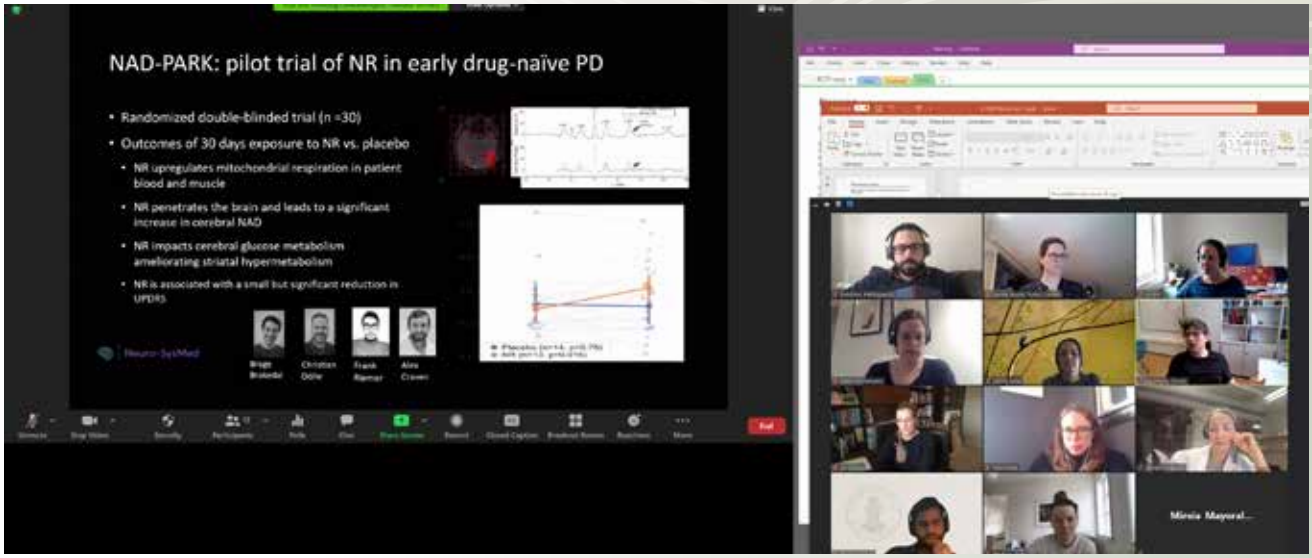
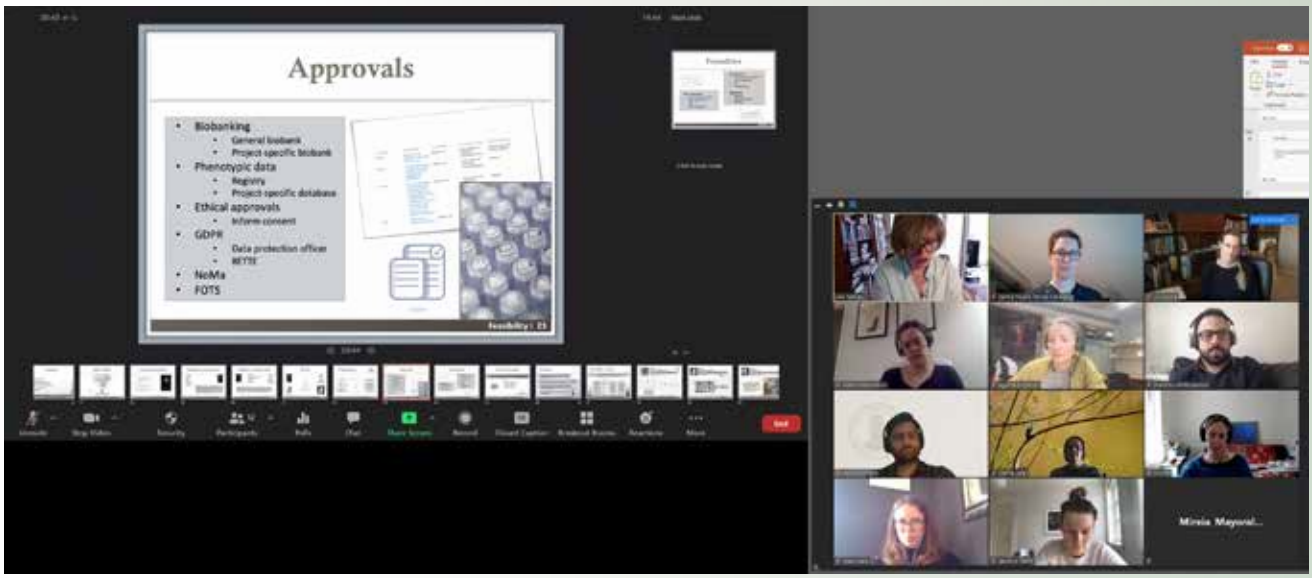
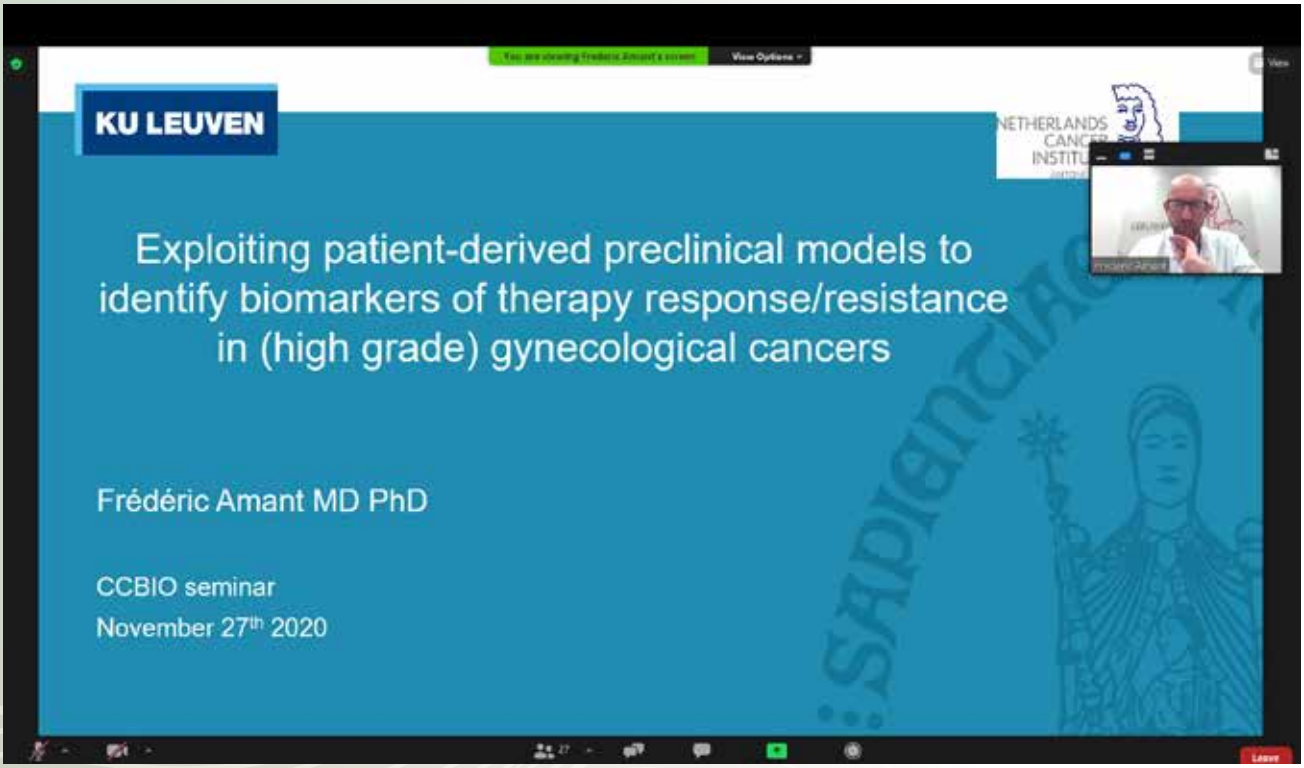

Is there NAD+ deficiency in PD?
NADH
NAD+
NAD+
Complex I deficiency
NAD+ deficiency
Sirtuin inhibition
Increased histone acetylation
Mireia Mayoral...


NAD-PARK: pilot trial of NR in early drug-naïve PD
• Randomized double-blinded trial (n =30)
• Outcomes of 30 days exposure to NR vs. placebo
• NR upregulates mitochondrial respiration in patient blood and muscle
• NR penetrates the brain and leads to a significant increase in cerebral NAD
• NR impacts cerebral glucose metabolism ameliorating striatal hypermetabolism
• NR is associated with a small but significant reduction in UPDRS
Mireia Mayoral...

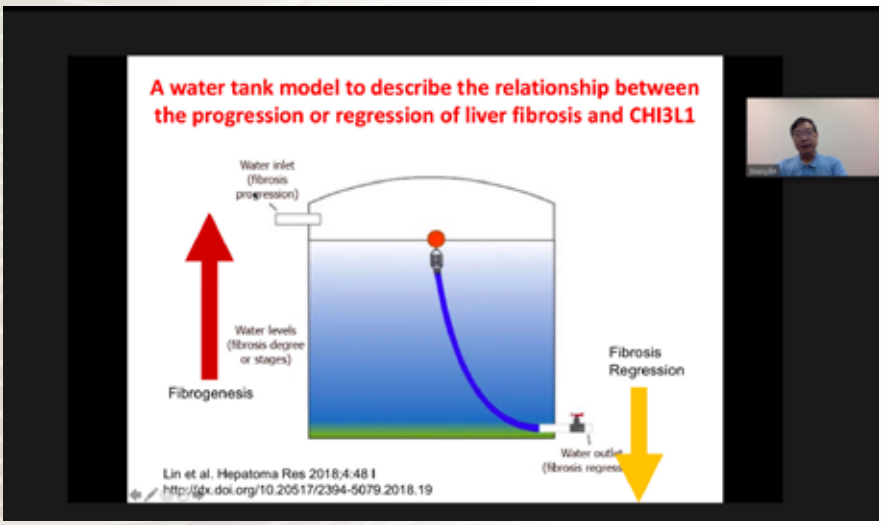

Approvals
• Biobanking
• Phenotypic data
• Ethical approvals
• GDPR
• NeMa
• FOTS
Mireia Mayoral...

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.

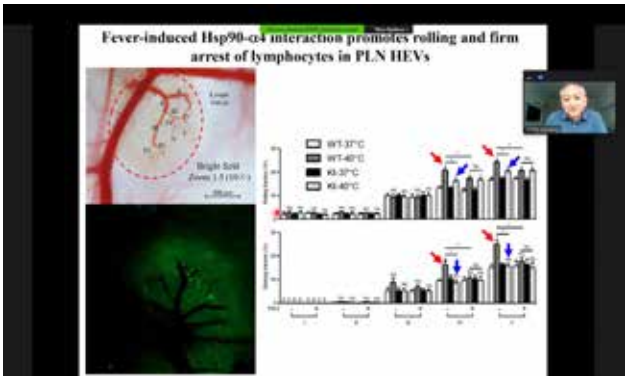
The aim of the seminar series is to convey relevant biomarker research to the local scientific community, also preparing the ground for future recruitment. In most cases, targeted meetings with the speakers are arranged before or after the lectures so that CCBIO's researchers, in particular the younger ones, get the opportunity to discuss projects and collaboration with high level researchers.



Normally, 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. In 2020, following the first COVID-related lockdown in March and April, CCBIO decided to run all seminars digitally until the end of the pandemic. This proved a success with good attendance, also from overseas collaborators and their staff. The reason for running the seminars purely on a digital platform also in the early autumn when the infection rate in Bergen was rather low,

is that CCBIO's researchers have affiliations and positions at a wide range of hospital departments, and an outbreak within CCBIO would therefore have dire consequences. The late autumn surge in infections, a renewed semi-lockdown, and instances of COVID-infections at hospitals proved this policy right. For the years to come, CCBIO hopes to profit from the increased level of digitalization by running its seminars with a flexible combination of online and on-site speakers and attendants.

The seminar series 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. Since the start in 2013, the collaboration with the BMED380 group has been a success, benefiting both parties. 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, and with this year's digital lectures, also from abroad. ••

CCBIO Research Seminars in 2020

JANUARY 30, 2020 // Johannes A. Eble, Institute of Physiological Chemistry and Pathobiochemistry, Cells in Motion Interfaculty Centre, University of Münster, Germany. Title: Beating around the bush yet hitting the point: CAFs and vasculogenic mimicry vessels as anticancer targets.

FEBRUARY 20, 2020 // Rameen Beroukhim, Dana-Farber Cancer Institute and Harvard Medical School, and Associate Member of the Broad Institute. Title: Ancestry-associated features in cancer.

MAY 28, 2020 // JianFeng Chen, Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences, Shanghai, China. Title: Regulation of immune cell trafficking by extracellular microenvironment.

JUNE 11, 2020 // Biaoyang Lin, Zhejiang University, China. Title: Critical roles of Chitinase 3-like 1 (CHI3L1) in inflammation, fibrosis and cancer.

AUGUST 27, 2020 // Ritva Heljasvaara, University of Oulu, Finland. Title: Novel roles of collagens and α11 integrin in solid cancers.

SEPTEMBER 24, 2020 // Joyce Bischoff, Harvard Medical School/Vascular Biology Program and Department of Surgery at Boston Children's Hospital, USA. Title: Endothelial Anomalies in Vascular Tumors and Vascular Malformations.

NOVEMBER 5, 2020 // Huocong Huang, Department of Surgery, University of Texas Southwestern Medical Center, Dallas, TX, USA. Title: Heterogeneity of cancer-associated fibroblasts in pancreatic cancer.

NOVEMBER 26, 2020 // Fréderic Amant, KU Leuven, Belgium and University of Amsterdam, the Netherlands. Title: Exploiting patient-derived preclinical models to identify biomarkers of response/resistance to therapy in (high grade) gynecological cancers.

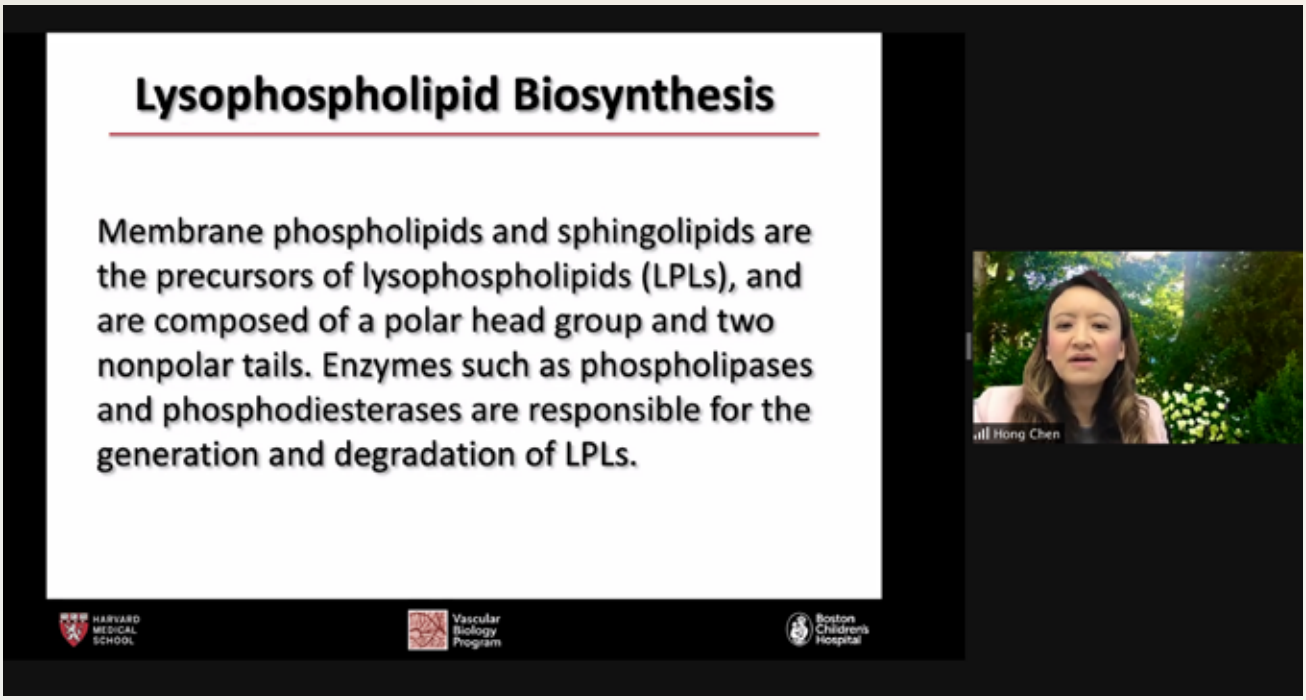
DECEMBER 17, 2020 // Jean Paul Thiery, Bioland Laboratory, Guangzhou Regenerative Medicine and Health, People's Republic of China. Title: Epithelial-mesenchymal transition in carcinoma; therapeutic intervention.

CCBIO Special Seminars and Mini-Symposia

When CCBIO members have senior researchers visiting or taking part in courses 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. Despite the COVID pandemic, 2020 ended up being a rather active year with a wide range of topics. As has been the case for in-person special seminars and mini-symposia, the online meetings in these formats were also well visited.

January 9, 2020 // Cancer in the News. CCBIO Special Seminar with an expert panel who discussed in depth the issue "Cancer in the news". Panelists were **Mille S. Stenmarck** and **Irmelin Nilsen** from the Centre for the Study of the Sciences and the Humanities at UiB, **Tine Dommerud** from Aftenposten, the largest newspaper in Norway, and **Knut Helland** from the Department of Information Science and Media Studies, UiB.

The panelists Stenmarck and Nilsen raised several points of reflection in their presentations. First, the dominant framings of cancer found in the news include those who convey great optimism towards cancer research – this field is often associated with ideas of "breakthroughs", "hope", "miracle medicines" or even "cures"; and those presenting suffering cancer patients who are denied "life-saving" medicines by the state. Second, these framings found in the news come from "socio-technical imaginaries" that are formulated by oncologists and other actors in the field of cancer research, where precision oncology is presented as a reality about to come true – it suffices to have the right technologies, enough funds and the political will to support that ideal. Third, these framings are not only wishful thinking, but also shape the way society conceptualizes cancer research and in particular precision oncology. They give the idea that there is no limit to what cancer research can provide. Tine Dommerud communicated some explanations as for why these framings

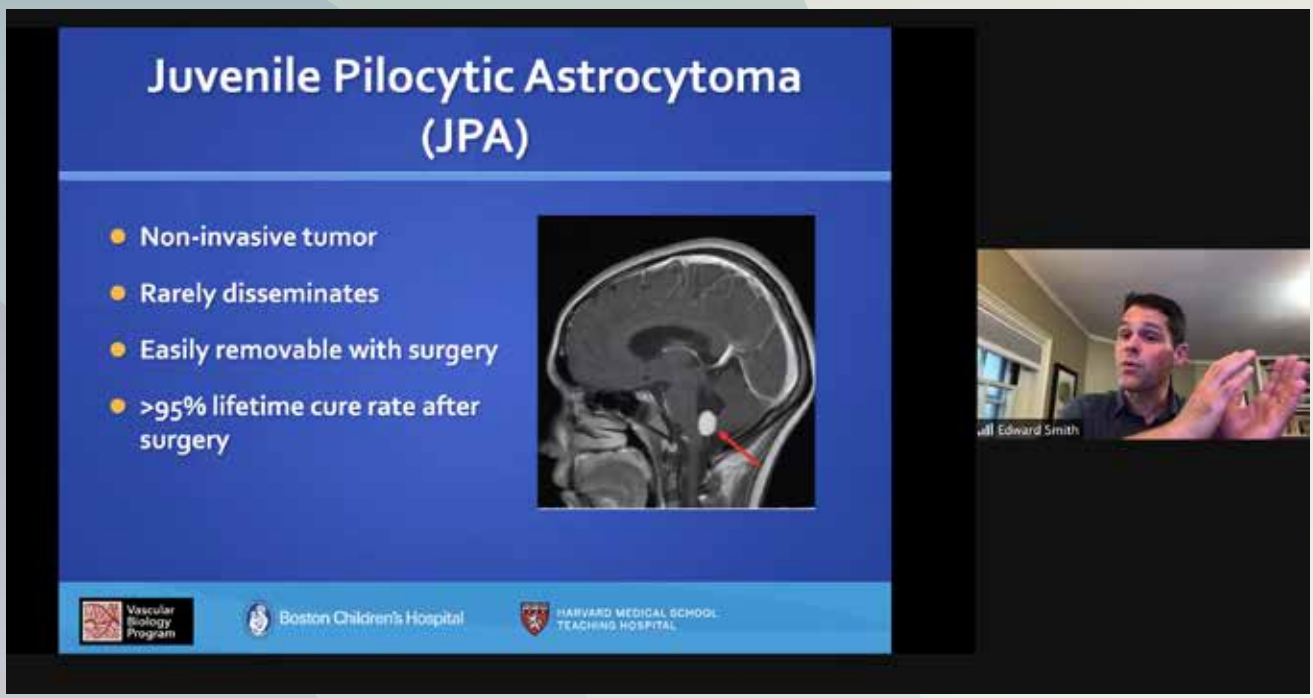


of cancer are present in the media, by uncovering some of the constraints that a newspaper has to work with. There is the assumed interest of the readership for stories that bring hope, and the difficulty to "sell" a story when it does not start from an individual's experience and struggles. There are also limited budgets and time, which means that some important and meaningful issues (like the pricing of drugs) are outside the scope of newspaper articles. Finally, there is the "tyranny or power of goodness", meaning that when something is assumed to be "good" (precision medicine for instance), it is extremely difficult to build a robust critical argument against it, that will not be rejected straight away by the readers.

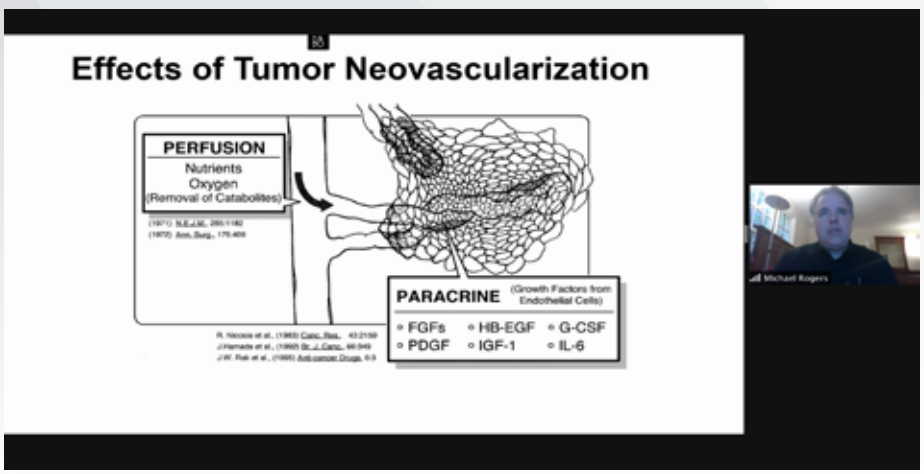
The diversity of backgrounds of the panelists allowed for a unique debate that critically reflected on how cancer is framed in the media today, whether this is a responsible media discourse, and what impact hope, enthusiasm and optimism has on society. This is a first step towards what Stenmarck and Nilsen argue for: ongoing, critical debates across society, science, politics and the media, on what responsible framings of and discourses around cancer are and should be.

January 31, 2020 // HyperTraPS: Learning pathways of disease (and cancer) progression from data. CCBIO Special Seminar with Iain Johnston, Department of Mathematics, University of Bergen. Mathematician **Iain Johnston** moved to Bergen in 2020 to work at the University of Bergen. Together with researchers from the Imperial College London, he has developed a new tool, HyperTraPS (hypercubic transition path sampling), with an algorithm that can uncover not only overall structures in how diseases develop, but also, based on a given set of symptoms, with a high probability predict the next stage of the disease course for each patient. Johnston explained how HyperTraPS can efficiently learn progression pathways from cross-sectional, longitudinal, or phylogenetically linked data, readily distinguishing multiple competing pathways, and identify the most parsimonious mechanisms underlying given observations. The tool has among other things been applied to data from thousands of ovarian cancer patients. The analyzes show different disease pathways that largely depend on which mutation came first. The study was published in Cell Systems in 2020.

September 28, 2020 // Endocytic Adaptor Protein Epsin is a Gatekeeper of the Quiescent Endothelium. CCBIO Special Seminar with speaker **Hong Chen**, Vascular Biology Program at Boston Children's Hospital and Harvard Medical School. She was the first to discover a family of important endocytic adaptor proteins, epsins (Chen et al., Nature, 1998, Chen et al., Proc. Natl. Acad. Sci. USA, 2003, 2005 and 2009). Her group developed a novel conditional epsin 1fl/fl; epsin 2-/- mouse, which has been pivotal to the group's continuous success by allowing characterization of the spatial and temporal roles of epsins. Impeding pathological angiogenesis associated with vascular disorders is paramount in treating disabling and deadly diseases such as blindness, diabetes and cancer. Epsins are a family of prominent endocytic adaptor proteins. Hong Chen explained how the group found that epsins, via their ubiquitin-interacting motifs (UIM), are critical for activated VEGFR2 internalization and degradation and VEGF signaling attenuation. Intriguingly, endocytosis of VEGFR2 via a different endocytic adaptor protein, Dab2, results in enhanced VEGF signaling. The group showed that epsins and Dab2 competitively interact with VEGFR2 via a mutually exclusive mechanism. Consequently, mice lacking epsins and Dab2 reduce heightened angiogenesis in

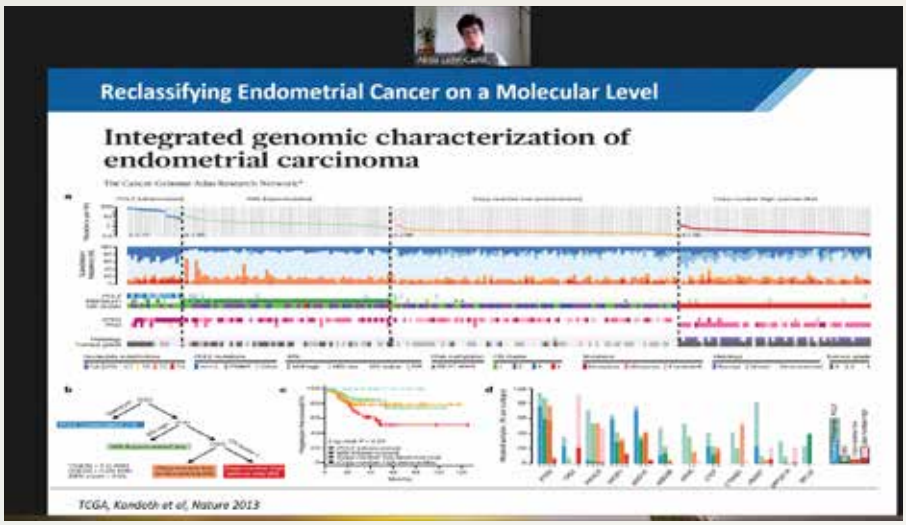


epsin mutants and restore attenuated angiogenesis in Dab2 mutants. However, whether the antagonism of epsins and Dab2 is governed by upstream signals, is poorly understood. The group's latest study revealed that Sphingosine 1 Phosphate (S1P) enhances epsins while reduces Dab2 binding to VEGFR2 to potentiate VEGFR2 degradation, implicating that S1P may be one of long-sought-after upstream cues that triggers epsin-mediated downregulation of VEGF signaling. Given that VEGF signaling plays a central role in normal, as well as pathological angiogenesis, their work to discover new molecules and pathways, in particular upstream signals and genetic modifiers that reign epsins' activity in regulating VEGF signaling and pathological angiogenesis, paves the way to develop new therapeutic approaches for the prevention and treatment of cardiovascular and other diseases.



September 30, 2020 // Learning from tumor to treat stroke. CCBIO Special Seminar with **Edward R. Smith**, Harvard Medical School, Boston Children's Hospital and Cerebrovascular Surgery and Interventions Center. He currently heads a translational research laboratory in the Vascular Biology Program with a focus on the development of non-invasive biomarkers and novel therapeutics for pediatric brain tumors and stroke. Along with Dr. Darren Orbach, he leads one of the largest pediatric cerebrovascular programs in the country, with a dedicated team focused on improving the outcomes of patients with moyamoya, aneurysms, arteriovenous malformations and cavernous malformations. Edward Smith's focus for the talk was how one of the most important abilities of teams involved in translational research is the capacity to recognize how a line of study in one field might impact a seemingly unrelated area. As an excellent example, he built on previous work that implicated a class of molecules – axonal guidance factors (AGFs) – in tumor development, and highlighted the thought process that led to investigating their role in a totally different field; stroke. Ultimately, the cross-pollination between benchtop scientists and full-time clinicians led to a unique insight that a shared biological mechanism might be pathologic in one disease process – and helpful in another, seemingly unrelated disease.

October 1, 2020 // Metastasis without a tumor. CCBIO Special Seminar with **Mike Rogers**, Harvard Medical School and Vascular Biology Program, Boston Children's Hospital. His major ongoing areas of research all relate to the role of angiogenesis and VEGF in disease pathology, including cancer, corneal neovascularization, and endometriosis. In mapping polymorphisms that affect the angiogenic response to bFGF and VEGF, he found (unexpectedly) that pigment production genes also affect blood vessel growth. Other current efforts include validation of anthrax toxin receptor 2 as a target for antiangiogenic therapy and identification of small molecule inhibitors of the protein, and identification of small-molecule antagonists of antizyme inhibitor. He has recently begun a substantial effort to identify novel therapeutic strategies for endometriosis-associated pain. To that end, his lab has developed and validated a mouse model of the condition and are currently evaluating novel targets to alleviate the suffering caused by the disease. Mike Rogers' main focus for this talk was metastasis, which has long been recognized as the most dangerous event in cancer progression, but which can occur in another context that has received much less attention: endometriosis. This condition is characterized by lesions that resemble ectopic endometrium and the leading hypothesis for its pathogenesis is metastatic spread following menstruation. Endometriosis is characterized by infertility and pain, with many patients poorly treated by existing therapies. The group's recently developed mouse model of endometriosis-associated pain has been validated using existing therapeutics and is now used to evaluate novel therapeutic hypotheses.



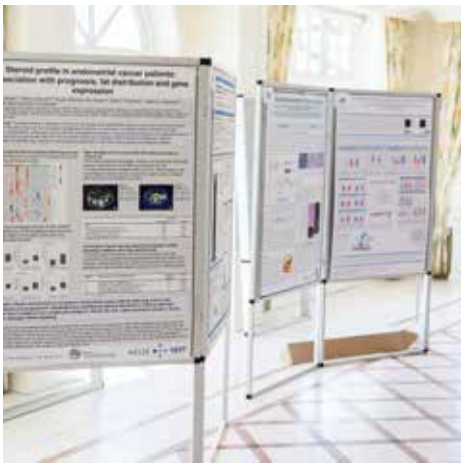
October 21, 2020 // Endometrial cancer - How will new molecular knowledge influence the way we are treating our patients? Mini-Symposium on endometrial cancer, with speakers **Alicia Leon del Castillo**, Leiden, **Alexandra Leary**, Paris; **Mansoor R Mirza**, Copenhagen; **Katrine Woie**, Bergen and **Ane Gerda Zahl Eriksson**, Oslo. Chairs were **Camilla Krakstad** and **Line Bjørge**. The incidence of endometrial cancer is rising both due to increased life-expectancy and higher degree of obesity in the population. Traditionally, endometrial cancer has been histologically classified and risk stratified based on clinico-pathological parameters. Molecular classification has the potential to replace histology for risk classification if solid molecular markers can be identified. The Cancer Genome Atlas (TCGA) endometrial cancer project described four distinct prognostic EC subtypes based on genomic abnormalities that reflect EC tumor biology: ultra-mutated, hyper-mutated, copy-number low and copy-number high subtypes. Subsequently, molecular and histopathologic classifiers have been suggested and evaluated for their prognostic and predictive value. The impact of molecular classification is evident and opens for development and use of more targeted therapies and will be recognized by the upcoming WHO classification. The Mini-Symposium focused on the current status for risk-stratification of endometrial cancer and highlighted the need for implementation of current knowledge in the clinic to improve treatment for endometrial cancer patients. **Alicia Leon del Castillo** held the talk "Histologic subtyping and grading, or Molecular classification? Endometrial cancer diagnosis in 2020." **Alexandra Leary** discussed endometrial cancer in the era of targeted therapy in her lecture, and

Mansoor R. Mirza presented the new ESGO guidelines for treatment of endometrial cancer. Norwegian representatives **Katrine Woie** and **Ane Gerda Zahl Eriksson** contributed with an overview of the new Norwegian guidelines for treatment of endometrial cancer. ••

8TH CCBIO ANNUAL SYMPOSIUM 2020

Each year in May, CCBIO normally arranges its annual symposium with around 200 participants or more from Norway and a wide range of international institutions. For the 2020 symposium, speakers and participants from all over the world were to be gathered May 12-13 to present and deliberate on recent advances within cancer research. We were looking forward to a broad range of talks by international experts which would have provided food for thought and new knowledge and ideas to bring home for everyone. Extended poster sessions would, as every year since 2013, have provided younger researcher with the best opportunities to discuss their science with their seniors as well as with each other.

The first pandemic lockdown due to COVID-19 was ordered by the Norwegian government on March 12, 2020, and this now seems a very long time ago. However, in the weeks leading up to May 2020, researchers' skills with online platforms were not yet at a level allowing for remote conferences at this scale. Sadly, the CCBIO Annual Symposium for 2020 had to be cancelled. Since then, we have not been idle, and multiple CCBIO courses, research seminars and other events have been successfully arranged online. For the 9th CCBIO Annual Symposium 2021, we have decided on a flexible format allowing for top notch keynote presentations online, several interactive panel discussions, and many presentations from young researchers since there would usually be poster presentations on-site. This will all take place regardless of whether we will arrange the symposium online only or as a combination of online talks and local physical participation at Solstrand. Therefore, we look forward to the CCBIO Annual Symposium May 18-19, 2021, and for the years to come! ••



Centre for Cancer Biomarkers

8th CCBIO Symposium 2020

Solstrand, May 12-13, 2020, Bergen, Norway

SPEAKERS AND TOPICS (CANCELLED)

ROBERT D'AMATO: The use of genome wide associations studies (GWAS) to identify novel genes which control angiogenesis in mice

SYLVIA K. PLEVRITIS: Optimizing drug combinations based on single cell resolution of intratumoral heterogeneity

RAMEEN BEROUKHIM: Hypermutation in gliomas

MARCO DAVILLA: The role of IL6 and myeloid cells with CD19-targeted CAR T cell clinical outcomes

MICHAEL ROGERS: What happens when an endothelial cell loses its compass? The role of CMG2 in angiogenesis

MALIN SUND: The effect of tumor stroma on pancreatic cancer treatment and diagnostics

KLAUS PANTEL: Liquid biopsy: From biology to clinical implementation

GUIDO SAUTER: Assessing cancer biomarkers by large-scale tissue analysis

MORAG PARK: Distinct tumor immune microenvironments stratify triple negative breast cancer

AMIR AREF: Patient derived organoids in cancer research

ANTONY BRAITHWAITE: Modulation of immune cell function by D133p53 isoforms

TUULA SALO: *In vivo* and *in vitro* models for planning personalized head and neck cancer treatment

MARIA LIE: Targeting AXL for increased anti-cancer immune surveillance

REIDUNN EDELMANN: AI-supported analyses of multi-marker-defined tumor vessels in clinical samples

DIMITRIOS KLEFTOGIANNIS: Multi-omics characterization of breast cancer cell-lines

ROGER STRAND (MODERATOR): Special session: Precision oncology: Issues at stake and matters of concern. Short presentations and discussion panel with co-authors of new CCBIO book project

Dissertations

It is always a joyous occasion when one of our PhD candidates defend their dissertation. The award of a PhD title is a celebration of the individual student's skills and long-term efforts, as well as an expression of a larger team effort, including supervisors, collaborators and support staff. It is also our strong impression that CCBIO's organized researcher training through the CCBIO Research School for Cancer Studies (RSCS) provides added substance and quality to the training of a PhD candidate. The RSCS is a scientifically stimulating and inclusive educational environment and meeting place for junior scientists within cancer research and with a common focus on translational studies of cancer biomarkers in the widest sense. It also serves as a bridge to CCBIO's ELSA efforts, providing future research leaders with important tools for research conduct and responsible decision making. During courses and other research school activities, PhD candidates and younger researchers meet and deliberate upon their research projects across the established groups. Through CCBIO's seminars, symposia and international faculty, our PhD candidates also get an unprecedented opportunity to interact with and establish collaborations with senior researchers internationally.

Throughout 2020, CCBIO had a total of 56 PhD candidates, of which 66% were female. 57% were of Norwegian origin and among the remainder, Africa and Asia were particularly well represented with about a third.

We congratulate the following 15 PhD candidates who successfully completed their doctoral work in 2020:

MARTIN PILSKOG
"Predictive biomarkers for response to treatment with sunitinib in renal cancer patients." Supervisors: Professor Oddbjørn Straume, Professor Christian Beisland and Professor Lars A. Akslen. Defense date: January 23, 2020.

HILDE RENATE ENGERUD
"Molecular markers to predict prognosis and guide therapy in endometrial cancer." Supervisors: Professor Camilla Krakstad and Professor Jone Trovik. Defense date: February 7, 2020.

TONE HOEL LENDE
"Proliferation in operable breast cancer. Aspects of prognostication and relevance of carbohydrate metabolism." Supervisors: Professor Håvard Søiland, Professor Emiel AM Janssen, Professor Emeritus Jan PA Baak and Professor Lars A. Akslen. Defense date: March 6, 2020.

JAHEDUL ALAM
"Novel Insights into Integrin α11 Expression and Function." Supervisors: Professor Donald Gullberg, Professor Rolf K. Reed and Professor James Lorens. Defense date: January 31, 2020.

CAROLINE BENEDICTE NITTER ENGEN
"Exploring the boundaries of precision haemato-oncology - The case of FLT3 length mutated acute myeloid leukaemia." Supervisors: Professor Bjørn Tore Gjertsen, Professor Emmet McCormack and Professor Øystein Bruserud. Defense date: February 14, 2020.

TORMOD KARLSEN BJÅNES
"Drug delivery in pancreatic cancer." Supervisors: Associate Professor Bettina Riedel, Professor Jan Schjøtt and Professor Emmet McCormack. Defense date: March 6, 2020.

HARSH NITIN DONGRE
"Biomarkers and preclinical models for more precise diagnosis and personalized treatment of oral and vulva carcinomas - Study on human samples and experimental models." Supervisors: Professor Daniela Elena Costea, Professor Line Bjørge and Professor Anne Christine Johannessen. Defense date: April 30, 2020.

HANNA ELISABETH DILLEKÅS
"Importance of physical trauma on recurrence of breast cancer. Can tissue trauma synchronize growth of dormant micrometastases?" Supervisors: Professor Oddbjørn Straume, Associate Professor Svein Arthur Jensen and Professor Olav Mella. Defense date: June 4, 2020.

RAGNHILD HAUGSE
"Endothelial cell signaling and sonoporation." Supervisors: Associate Professor Spiros Kotopoulis, Professor Emmet McCormack and PhD Anika Langer. Defense date: June 17, 2020.

YAPING HUA
"Discovery and characterization of novel STAT3 and androgen receptor inhibitors in prostate cancer cells." Supervisors: Professor Karl-Henning Kalland and Professor Xisong Ke. Defense date: May 5, 2020.

EDUARDA GUERREIRO
"Isolation and characterization of extracellular vesicles – Molecular couriers from cancer cell lines, and saliva and tear fluid from patients with primary Sjögren's syndrome." (UiO/UiB). Supervisors: Associate Professor Tine Merete Søland and Professor Daniela Costea. Defense date: June 12, 2020.

NAZAR GAFAR ABDULRAHMAN MOHAMED
"Biomarker Identification in Oral Squamous Cell Carcinoma. Study on Cohorts of Patients from Sudan." Supervisors: Professor Daniela Elena Costea, Professor Anne Christine Johannessen, Professor Ahmed Sulaiman and PhD Elisabeth Sivy Nginamau. Defense date: June 19, 2020.

SISSEL DYRSTAD
"A study on metabolic rewiring in cancer cell plasticity." Supervisors: Professor Karl Johan Tronstad, Researcher Gro Vatne Røsland and Professor Jim Lorens. Defense date: August 21, 2020.

EHSAN HAJJAR
"Next generation leukemia diagnostics and therapy through p53 isoforms." Supervisors: Professor Bjørn Tore Gjertsen, Senior Researcher Vibeke Andresen and Advisor Sigrun Margrethe Hjelle. Defense date: December 17, 2020.

MIKYUNG KELLY SEO
"Economic evaluations of companion cancer biomarkers for targeted therapies." (UiB/London School of Hygiene and Tropical Medicine.) Supervisors: Professor John Cairns and Dr. Alec Miners. Defense date: November 20, 2020.

FACTS AND FIGURES 2020

CCBIO's scientific production is high, and the spike in publications during 2016-2017 was due to the first round of CoE financed PhDs and postdocs concluding their projects those years. The influx of external funding is good. The numbers listed reflect the funds consumed each year, not funding granted. Due to the pandemic related shutdown of laboratories in 2020 causing a slump in research activity, and a complete stop of in-person attendance at meetings and conferences, less funds were used than anticipated. For a CoE within cancer research, CCBIO is very active in terms of outreach with a substantial amount of mass media appearances.

PERFORMANCE INDICATORS

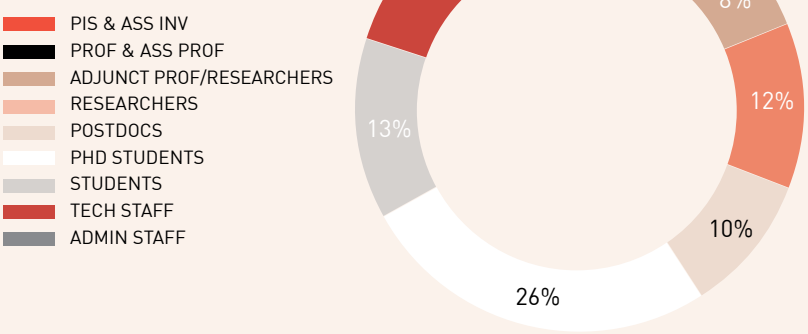
	2013	2014	2015	2016	2017	2018	2019	2020	TOTAL
PUBLICATIONS	76	71	77	85	94	81	79	79	642
COMPLETED PHDS	5	6	3	10	12	9	8	15	68
EXTERNAL FUNDING MNOK	7.2	21.9	22.5	36.0	34.0	32.1	26.7	30.0	210
MEDIA APPEARENCES	39	11	32	31	54	40	68	54	329

GENDER DISTRIBUTION
(HEADCOUNT)

TOTAL: 217 PERSONS

Among the 217 persons involved in the CCBIO enterprise, there is a clear overall majority of women. Of our PhD candidates and postdocs, two thirds are female. The female share among senior scientific staff is steadily increasing and is now on 44%. CCBIO's active recruitment of excellent female staff during its second CoE period has increased the female proportion of its principal and associate investigators to 27%. CCBIO wishes to underline that no affirmative action has been taken at any point, and recruitment is done purely on merit. Among more junior staff and future group leaders, perceived potential is also considered. At the same time, CCBIO is confident that a gradually improving gender balance in its top tire will ensure the available talent being put to its best use and result in improved output.

CCBIO STAFF OVERVIEW
(HEADCOUNT)

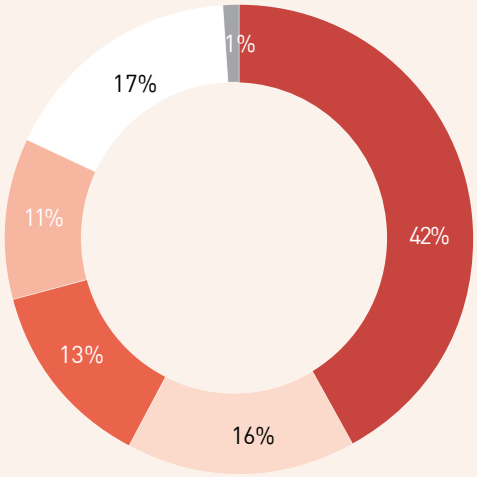


TOTAL: 217 PERSONS

CCBIO has a balanced composition of junior and senior researchers, technicians, and administrative support staff. To better prepare the ground for major breakthroughs and high-level publications, the center has decided to focus even more strongly on recruiting postdocs rather than PhDs for the remainder of its CoE period. CCBIO has also recruited younger and predominantly female principal and associate investigators. To prepare CCBIO's future group leaders, we are currently training several selected researchers in the skills they will need as group leaders (the CCBIO Masterclass Program). The CCBIO International Faculty network of 14 top notch affiliated professors and researchers ensures excellent access to high-level collaboration, advice, and tuition for CCBIO's senior researchers, younger researchers, and PhDs, respectively.

FUNDING
(FUNDS USED IN 2020)

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

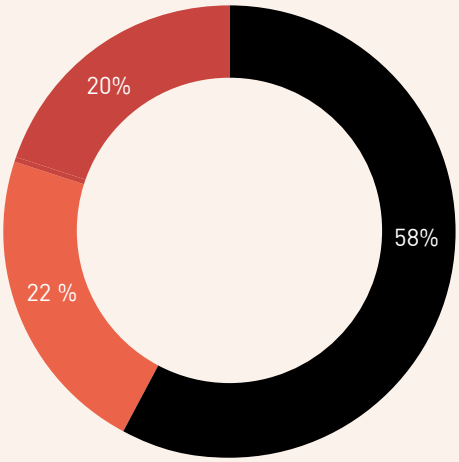


TOTAL: 72.3 MILL NOK

As abruptly interrupted experiment series take time to reinitiate, the pandemic related lockdown of laboratories had consequences far beyond the initial phase. This, in addition to cancellation of in-person meetings, naturally effected the rate at which funds were used in 2020. We expect the consumption of financial resources to increase in step with CCBIO's effort to regain lost ground in the years to come. Total funds used in 2020 were 72,3 MNOK, of which 16,2% is the RCN CoE funding and 42,2% is funding from the UiB. The external funding consumed was 41,6%. Despite the pandemic related reduction in funding used, this is twice the budgeted amount and illustrates a high success rate with public and private funding agencies, as well as CCBIO's effort to regain momentum.

INTERNATIONALIZATION
(STAFF COUNTRY OF ORIGIN)

- NORWAY
- OTHER WESTERN COUNTRIES
- AFRICA & ASIA

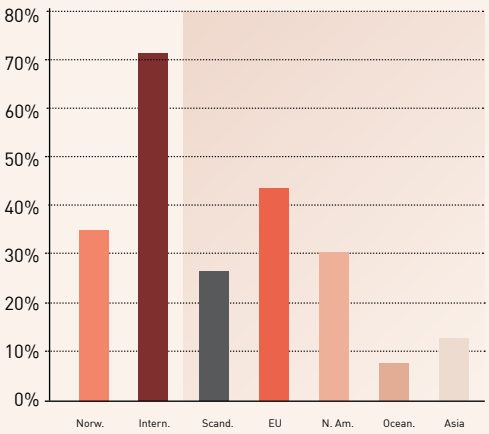


TOTAL: 217 PERSONS

CCBIO is an international CoE with 42% of its overall staff having other citizenships than Norwegian, and 43% and 62% of its PhDs and postdocs originate from outside of Norway. In both latter categories, a clear majority of the international staff originates from Asia and Africa. Among CCBIO's senior researchers, 42% are foreign nationals, mainly due to CCBIO's recruitment of a predominantly international network of top tire researchers to adjunct positions.

INTERNATIONALIZATION
(STAFF CO-AUTHORSHIP)

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



CCBIO's large international research network, both formalized and in terms of scientific collaboration, has generated a substantial number of scientific publications with international contributors. In 2020, 71% of CCBIO's publications had co-authors with institutional affiliation abroad, a clear increase from 58% in 2019. Interestingly, international co-authorship has much stronger prevalence than collaborations with researchers from other Norwegian universities (35% of publications). Subdividing the international co-authorships into regions (shaded background) demonstrates that CCBIO collaborates with institutions from most major regions worldwide. The keen observer will notice that the aggregate value of the five columns to the right reach around 120%. By comparing this total with the "International over all"-column, one can discern that many of CCBIO's international publications have co-authors from more than one region, being truly multilateral collaborations.

Dissemination and Communication 2020

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 issues a newsletter at regular intervals (6 issues per year) and 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 dissemination and communication efforts in 2020:

CCBIO in a Nutshell; Release of a 1 minute' synopsis of CCBIO's focus and activities, in a popular science language. The film featured at the annual conference of Digital Life Norway and was shared through Facebook and other media and partners websites.

YouTube entry of Personalized Medicine for Acute Myeloid Leukemia (AML); Short video where Postdoc Dimitrios Kleftogiannis in the Jonassen group explains their use of machine learning and mathematical modeling to develop classification systems for AML with single cell resolution. Also shared on other social media.

Panel debate about the University's new open science policy. CCBIO Associate PI Camilla Krakstad contributed as one of the panelists in the seminar, with audience both in the room and through a digital platform.

Promoting new research: Tweet disseminating info on research results from the Kalland group.

Facebook entry about former CCBIO PI and current CCBIO Strategic Advisor, Rolf K. Reed, who October 14 was awarded with the prestigious Norwegian award the King's Medal of Merit, presented to him by the Mayor of Bergen.

Public meeting in March 2020 on the topic "The mythology of cancer: the solution to cancer". Arranged by Filosofisk poliklinikk, chaired by Caroline Engen, board member of Filosofisk poliklinikk, MD and a PhD graduate affiliated to CCBIO. Key speaker was Jarle Breivik, professor at the Department of Medical Behavioral Sciences in Medicine at the University of Oslo. Jarle Breivik has previously provoked leading cancer researchers with the article "We Won't Cure Cancer," published in The New York Times.

Tweet about Researcher Stein-Erik Gullaksen in the Gjertsen group who received the Incyte Nordic Grant for Hematological Research for the year 2020.

Facebook entry promoting an open CCBIO Special Seminar with a panel debate on the topic Cancer in the News.

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 highly interactive performances and lectures on cancer and biomarkers to schools on CCBIO's behalf. In 2020, 279 schoolchildren in the Bergen area got to experience the tumor microenvironment on stage through 9 performances in schools and other arenas before the COVID-19 lockdown.

MEDIA APPEARANCES


Bergens Tidende BT Magasinet Sport Økonomi Menin

Gode resultater for bergensk kreftvaksine

29. desember 2020 kl 16:12 av Kari Pedersen

DEL

Utprøving av fryseterapi startet for seks år siden. Christian Beisland, Karl-Henning Kalland, Anne Margrethe Øyan og Alfred Honoré, viser frem maskinen som frysør ned kreftsvulsten. Foto: Eirik Brokke (arkiv)

DECEMBER 29, 2020 – BERGENS TIDENDE
"Gode resultater for bergensk kreftvaksine"
– Karl-Henning Kalland

DECEMBER 21, 2020 – FREMTIDEN
"Fylkeslegen med tilsynssak mot laserklinikk:
– Vi følger alle regler" – Oddbjørn Straume

DECEMBER 12, 2020 – KHRONO
"På tide å sette av fem prosent av prosjektmidlene til datahåndtering?" – Inge Jonassen


Medisin Nyheter Debatt Pharma DM Arena DMTV Om oss

Forskning på leukemi: – En rivende utvikling

Det skjer mye innen forskningen på behandlinger som kan brukes ved akutt myelogen leukemi, mener forsker Bjørn Tore Gjertsen

DECEMBER 8, 2020 – DAGENS MEDISIN
"Forskning på leukemi: – En rivende utvikling"
–Bjørn Tore Gjertsen

DECEMBER 8, 2020 – DAGENS MEDISIN
"Norskutviklet behandling med effekt i kombinasjon med cellegift" – Bjørn Tore Gjertsen

DECEMBER 6, 2020 – DAGENS MEDISIN
"Forsker på mulig immunterapi for minimal restsykdom"
– Bjørn Tore Gjertsen

NOVEMBER 16, 2020 – FORSKNING NO
"Norsk forskning gir håp: Blodkreft-rammede kan få mindre bivirkninger" – Stein-Erik Gullaksen

NOVEMBER 12, 2020 – EUREKALERT!
"University of Iowa virology research helps facilitate new clinical trial for COVID-19"– Jim Lorens

Medisin

Nyheter Debatt Pharma DM Arena DMTV Om oss

Norsk forsker hedret med stipend for sin forskning på blodkreft

Stein-Erik Gullaksen, forsker ved Universitetet i Bergen, har vunnet et stipend på 200.000 kroner for sin forskning på kronisk myelogen leukemi (KML). – Dette stimulerer til viktig forskning som ellers kanskje ikke er mulig, sier Gullaksen.

NOVEMBER 3, 2020 – DAGENS MEDISIN
"Norsk forsker hedret med stipend for sin forskning på blodkreft"– Stein-Erik Gullaksen

OCTOBER 28, 2020 – INCYTE
"Norsk forsker prisbelønnet for forskning på kronisk myelogen leukemi"– Stein-Erik Gullaksen

OCTOBER 26, 2020 – DAGENS MEDISIN
"Genotyping kan gi færre bivirkninger ved kreftbehandling" – Tormod Karlsen Bjånes

OCTOBER 19, 2020 – PÅ HØYDEN
"Kongeleg heder til UiBere" – Rolf K. Reed

Kongeleg utmerking til akademisk bauta

Det var duka for superlativ og stas då professor Rolf Reed ved Det medisinske fakultet fekk utdelt Kongens fortenestemedalje.

OCTOBER 14, 2020 – UIB NYHETER
"Kongeleg utmerking til akademisk bauta" – Rolf K. Reed

Medisin

Nyheter Debatt Pharma DM Arena DMTV Om oss

Forsker på nøyaktig fjerning av svulstvev ved eggstokkreft

Målrettet kirurgisk fjerning av svulstvev er gjenstand for nye studier - der kirurgen får hjelp til å se det øyet ikke ser.

Eggstokkreft er den nest hyppigste formen for underlivskreft i den vestlige verdensdelen.

I Norge blir 500 kvinner diagnostisert med sykdommen hvert år. Sykdommen har ofte spredd seg på diagnosetidspunktet. Prognosen er dårlig, og færre enn 45 prosent blir kurerte.

Det er tidligere vist at det er sammenheng mellom mengde gjenværende svulstvev og hvilken prognose pasienten har ved primær kirurgi.

I en studie som ble lagt frem under kreftkongressen ASCO for sommeren, fant man at pasienter som fikk en kombinasjonsbehandling som beste av kirurgi og standard cellegift, tok det lengre tid før sykdommen kom tilbake.

Disse pasientene levde også syv måneder lenger enn dem som

OCTOBER 8, 2020 – DAGENS MEDISIN
"Forsker på nøyaktig fjerning av svulstvev ved eggstokkreft" – Line Bjørge, Emmet McCormack

SEPTEMBER 19, 2020 – ALT OM DIN HELSE
"Nye, gode medisiner ved akutt myelogen leukemi" – Bjørn Tore Gjertsen

AUGUST 26, 2020 – HEALTHTALK
"Ny studie: Pasienter med en aggressiv blodkreftsykdom lever lenger med ny behandling" – Bjørn Tore Gjertsen

Dagbladet

PLUSS

Blodprøven som kan avsløre kreft

Ved hjelp av blodprøver, kan forskerne oppdage kreft hele åre år før svulsten er synlig. - Dette kommer til å revolusjonere måten man tenker på testing, sier kreftoverlege.

BLODPRØVE: Ny forskning kan bidra til at kreft blir oppdaget så tidlig som mulig.

AUGUST 5, 2020 – DAGBLADET
"Blodprøven som kan avsløre kreft" – Bjørn Tore Gjertsen

JUNE 11, 2020 – DAGENS MEDISIN
"Mener ny behandling ikke bare kan drives av de mest entusiastiske legene"
– Line Bjørge

JUNE 11, 2020 – DAGENS MEDISIN
"Overlevelses-gevinst på 12 måneder" – Line Bjørge


Khrono

Støtter anbefalinger om Sentre for fremragende forskning (SFF)

Vi støtter fullt ut evalueringskomiteens analyser og anbefalinger, skriver 41 ledere av eksisterende og tidligere SFF-er.

JUNE 4, 2020 – KHRONO
"Rapporten om ordningen med SFF er klar. Vi er takknemlige for komiteens omfattende og grundige arbeid" – Lars A. Akslen

JUNE 4, 2020 – LMI
"Diskuterte mulighetene for nye prioriteringssystemer i helsetjenesten" – Ole Frithjof Norheim


Medisin

Nyheter Debatt Pharma DM Arena DMTV Om oss

Foreslår ekspertgruppe

UiB-professor Ole Frithjof Norheim synes kritikken av alvorlighetsgrupperingen er god og legitim. Han foreslår en ekspertgruppe for å lage et mer nyansert system.

JUNE 3, 2020 – DAGENS MEDISIN
"Foreslår ekspertgruppe" – Ole Frithjof Norheim

JUNE 2, 2020 – DAGENS MEDISIN
"Norge aktivt med på ASCO" – Line Bjørge

JUNE 1, 2020 – DAGENS MEDISIN
"Se livestream: Ekspertene oppsummerer årets høydepunkter fra ASCO" – Line Bjørge


Medisin

Nyheter Debatt Pharma DM Arena DMTV Om oss

Innledning

Bergensforskere la frem resultater fra forskning på ny form for immunterapi

Kryoimmunterapi-prosjektet i Bergen har gjennomført en sikkerhetsstudie på behandling av pasienter med prostatakreft.

JUNE 1, 2020 – DAGENS MEDISIN
"Bergensforskere la frem resultater fra forskning på ny form for immunterapi" – Liv Cecilie Vestrheim Thomsen

MAY 29, 2020 – DAGENS MEDISIN
"100 kvinner i året kan få tilbud om kreftkirurgi mot tilbakefall" – Line Bjørge

MAY 23, 2020 – BERGENS TIDENDE
"Silikon-problemer sa legene da Waneska fikk kul i brystet" – Oddbjørn Straume

MAY 22, 2020 – KHRONO
"Filosofar meir relevante enn på lenge" – Ole Frithjof Norheim

MAY 20, 2020 – KHRONO
"Suksess med seks milliarder til fremragende forskning" – CCBIO


frontiers in Immunology | Cancer Immunity and Immunoth

Editorial: Targeting the Tumor Microenvironment for a More Effective and Efficient Cancer Immunotherapy

MAY 15, 2020 – FRONTIERS IN IMMUNOLOGY
"Editorial: Targeting the Tumor Microenvironment for a More Effective and Efficient Cancer Immunotherapy"
– James Lorens


Alvorlig syk lungekreftpasient fikk Bergenbio-medisin. Da hun fikk korona, slapp hun unna med litt feber.

Eldre kvinne med lungekreft hadde i 18 måneder tatt medisinen til Bergenbio. Da hun fikk covid-19, slapp hun unna med hodepine og feber i tre dager.

APRIL 30, 2020 – BERGENS TIDENDE
"Alvorlig syk lungkreftpasient fikk BerGenBio-medisin. Da hun fikk korona, slapp hun unna med litt feber"
– Hani Gabra

APRIL 29, 2020 – MEDFAK NEWS
"Bergenbio-legemiddel kan bli korona-medisin"
– James Lorens


Forskarar fann 109 nye risiko-gen for føflekkreft

Pasientar frå Bergen inngår i den store internasjonale studien. UiB-professor Lars A. Akslen håper funna på sikt kan bidra til betre behandling av føflekkreft.

APRIL 28, 2020 – BERGENS TIDENDE
"Forskarar fann 109 nye risiko-gen for føflekkreft"
– Lars A. Akslen

APRIL 27, 2020 – DAGENS MEDISIN
"Ja til legemidler mot kreft og sepsis" – Line Bjørge


Tidsskriftet

Need for change in cancer follow-up

The COVID-19 pandemic has given new relevance to the way in which cancer patients are followed up. There are good reasons for making the changes that are now being introduced permanent.

APRIL 21, 2020 – TIDSSKRIFT FOR DEN NORSKE LEGEFORENING
"Need for change in cancer follow-up" – Line Bjørge

APRIL 20, 2020 – TIDSSKRIFT FOR DEN NORSKE LEGEFORENING
"Kreftoppfølgingen bør endres" – Line Bjørge

APRIL 6, 2020 – BERGENSAVISEN PLUSS
"Folkehelsen vil lide om andre pasienter ikke prioriteres"
– Ole Frithjof Norheim

APRIL 5, 2020 – BERGENSAVISEN
"Mener andre nå bør prioriteres" – Ole Frithjof Norheim


Dagens Medisin

Nyheter Debatt Pharma DM Arena DMTV Om oss

Ingen rettferdige priser uten mer åpenhet

Norge kan støtte opp om WHO-resolusjonen gjennom å kreve større åpenhet om utviklingskostnader og priser for nye legemidler – for sjeldne som for andre sykdommer.

Eirik Joakim Tranvåg Kristine Husøy Onarheim

Innlegg: **Eirik Joakim Tranvåg**, lege og doktorgradsstipendiat i Bergen senter for etikk og prioriteringer (BCEPS) ved Universitetet i Bergen (UiB).
Kristine Husøy Onarheim, lege og postdoktor ved University College, London

ADMINISTRERENDE DIREKTØR John-Arne Rettingen i Norges forskningsråd mener Norge bør være villig til å betale mer for legemidler mot sjeldne sykdommer. Uten åpenhet om de faktiske utviklingskostnadene og prisene for legemidler mener vi det gir liten mening å snakke om rettferdig prising og solidaritet.

MARCH 29, 2020 – DAGENS MEDISIN
"Ingen rettferdige priser uten mer åpenhet"
– Eirik Joakim Tranvåg

MARCH 27, 2020 – HEALIO
"Researchers develop AI-based projects for tumor scoring, vessel annotation" – Reidunn Edelmann

MARCH 24, 2020 – AFTENPOSTEN
"Rangering av helsehjelp er en av de vanskeligste etiske utfordringene vi kjenner" – Ole Frithjof Norheim

MARCH 20, 2020 – DAGENS MEDISIN
"Prioritering: – Må opprettholde idealet om likebehandling"
– Ole Frithjof Norheim


BioTechniques

Liesbeth Hondelink and Reidunn Jetne Edelmann on deep learning for cancer research and early career advice for women in STEM

MARCH 5, 2020 – BIOTECHNIQUES
"Liesbeth Hondelink and Reidunn Jetne Edelmann on deep learning for cancer research and early career advice for women in STEM" – Reidunn Edelmann

MARCH 1, 2020 – NORD24
"Lytix Biopharma med nye lovende studier for kreftmedisin"
– Nina Louise Jebsen


Hvordan har kvinner med eggstokkreft det – egentlig?

FEBRUARY 2020 – BERGEN SANITETSFORENING
"Hvordan har kvinner med eggstokkreft det – egentlig?"
– Line Bjørge, Karen Rosnes Gissum, Roger Strand

FEBRUARY 13, 2020 – DAGENS MEDISIN
"Etikken - og hensynet til det enkelte mennesket"
– Ole Frithjof Norheim

FEBRUARY 9, 2020 – BERGENSAVISEN PLUSS
"Ny, lovende medisin avslører kreftsvulster"
– Nina Louise Jebsen

FEBRUARY 8, 2020 – THE CHINA POST
"Cancer research: Could drugs already on the market provide a cure?" – Karl-Henning Kalland

FEBRUARY 7, 2020 – AMED POST
"Cancer research: Could drugs already on the market provide a cure?" – Karl-Henning Kalland

FEBRUARY 4, 2020 – DW ACTUALIDAD
"Buscando medicamentos contra el cáncer en el botiquín"
– Karl-Henning Kalland


DW Made for minds.

THEMEN MEDIA CENTER TV DEUTSCH LERNEN

Das Medikament hilft auch gegen Krebs?

FEBRUARY 3, 2020 – DEUTSCHE WELLE
"Das Medikament hilft auch gegen Krebs?"
– Karl-Henning Kalland

MINI BIOGRAPHIES

PhD Candidates, Postdocs and Researchers 2020

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

ANANDAN, SHAMUNDEESWARI
MS in biotechnology and is currently a PhD candidate in the Bjørge and McCormack groups. Her research focus is on 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.

ANDRESEN, VIBEKE
PhD in molecular biology from the University of Bergen followed by a 5-year postdoc period at the National Cancer Institute, NIH, USA, a second postdoc period at the University of Bergen and then a researcher position through the Trond Mohn Foundation. She is currently a senior researcher in the Gjertsen group. Her focus is translational research in acute myeloid leukemia (AML), from the discovery of effective drugs and mapping of their molecular mechanisms and biomarkers to translation into clinical trials.

ASKELAND, CECILIE
MD from the University of Bergen and works as a senior 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.

BENTSEN, PÅL TORE
MD from the University of Bergen and is 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 resistance. 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 and is currently a PhD candidate in the Krakstad group. Her main research focus is to establish an organoid-based preclinical platform for endometrial cancer research. Preclinical models will be used to increase the understanding of endometrial cancer biology and to identify promising treatment strategies.

BJØRNSTAD, OLE VIDHAMMER
MS in biomedicine from the University of Bergen. He is currently a PhD candidate in Akslen's group, supervised by Heidrun Vethe and Lars A. Akslen. His PhD project focuses on different aspects of breast cancer stem cell biology and tumor microenvironmental interactions, with special emphasis on nerves.

BJÅNES, TORMOD KARLSEN
MD and senior consultant in clinical pharmacology at Haukeland University Hospital. He completed his PhD in March 2020. The work focused on drug delivery and intracellular pharmacokinetics in pancreatic cancer and included *in vitro* and clinical studies of the nucleoside analogue gemcitabine combined with sonoporation, performed in collaboration with the McCormack group.

BOUGNAUD, SEBASTIEN
MS in biology (specialty neuroscience) from the University of Strasbourg, and a PhD on brain tumors from the NORLUX Neuro-Oncology Laboratory (CRP-Santé) in Luxembourg. He was a postdoc in the Lorens group between 2014-2017, studying tumor/stroma dynamics *in vivo* during different phases of breast and lung cancer. As a researcher between 2017-2020, he led three sponsored research (SR) projects with BerGenBio ASA and the Lorens group at CCBIO that evaluated new therapeutic concepts for AXL targeting in cancer, where they demonstrated that AXL inhibition potentiates the immune checkpoint blockade in two different murine models of cancer.

BREMER, ANNE (NÉE BLANCHARD)
Holds a PhD on interdisciplinarity related to climate change and has a particular interest in the complex science-policy interface and the role of science in society. She was a postdoc in the Strand group, focusing on ethical, legal and societal aspects of cancer biomarkers. Bremer is currently a researcher in the same group continuing her postdoc work, aiming to create reflexive and dialogic spaces within CCBIO to discuss issues related to precision oncology. In particular, she has co-organized the CCBIO903 PhD course, and edited together with Roger Strand the book *Cancer Biomarkers: Ethics, Economics and Society* (Megaloceros Press, 2017). She is currently co-editing the upcoming follow-up volume: *Precision Oncology and Cancer Biomarkers: Issues at stake and matters of concern.*

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

CHEN, YING
MD, pathologist and currently medical director at Fürst Medical Laboratory (Oslo). She is since 2015 a part-time PhD candidate in the Akslen group, supervised by Lars A. Akslen, Tor-Audun Klingen, and Elisabeth Wik. Her PhD project focuses on breast cancer stroma and aims to identify the interplay between tumor-infiltrating lymphocytes, vascular invasion and stromal elastosis.

D'MELLO, STACEY
PhD in molecular medicine from the University of Auckland. She is 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.

DAS, RIDHIMA
Certified dental surgeon from India with an MS in experimental oral pathology from Queen Mary University London, UK. She is currently a PhD candidate in the Costea group, and her research project is focused on novel methods and sources for regeneration of oral mucosa.

DE GARIBAY, GORKA RUIZ
PhD in biochemistry from the Complutense University of Madrid. From 2017 to 2020, he was a postdoctoral researcher in the McCormack group. His research focused on the development of preclinical models of pancreatic ductal adenocarcinoma derived from patients.

DHAKAL, SUSHIL
MS in biomedical sciences from the University of Bergen. He is currently a PhD candidate 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 was a PhD candidate in the Straume group until completing her degree in June 2020. Her PhD work 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
PhD from the University of Bergen focusing on the role of microRNAs in progression of squamous cell carcinomas. Since November 2020, he is a postdoc in Costea and Bjørge groups on differential mechanisms of tumor-stroma interactions in human papilloma virus (HPV) positive and HPV negative carcinomas.

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

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

EHSANI, REZVAN
MS in mathematics from the University of Sistan and Baluchestan, Iran and a PhD in bioinformatics from NTNU Norway, focusing on computational methods on gene regulation at the level of transcription. Currently he is a postdoc with the Computational Biology Unit (CBU) in the Jonassen and Akslen groups. He is focusing on analyzing tumor microenvironment data from the Hyperion Imaging System to generate spatial information on sub-cellular resolution on protein abundance in and around tumors.

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

ENGELSEN, AGNETE
Cand. scient. in cell and developmental biology and a PhD in biomedicine from the University of Bergen. Since 2013 she has been affiliated with CCBIO, first as a postdoc in Lorens' group, and later as a visiting researcher at the Gustave Roussy Cancer Center Grand Paris (France). She was the project leader of the project "Impact of epithelial plasticity programs on anti-tumor immune-response". Agnete is currently a researcher in the Lorens group, establishing a non-small cell lung cancer patient derived organoid model recapitulating the complex tumor-immune microenvironment.

ENGEN, CAROLINE BENEDICTE NITTER
MD from the University of Bergen, and a PhD candidate 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 the University of Bergen. 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 a PhD in the field of neuro-oncology, both from the University of Bergen. She is since late 2018 a postdoc in the Krakstad group, with a focus on functional imaging of endometrial cancer mouse models.

FONNES, TINA
VMD from The Norwegian University of Life Sciences and a PhD from the University of Bergen. Her PhD work was performed in the Krakstad group and focused on preclinical models and molecular biomarkers – tools to improve treatment in endometrial carcinoma. She worked as a postdoc in the same group until June 2020, focusing on preclinical models for endometrial cancer.

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

GABRIEL, BENJAMIN
PhD from the Robert Koch Institute in Berlin, and a doctorate from Freie Universität in Berlin, followed by a 5-year postdoctoral residency at the University of Rhode Island, with a focus on the T-cell repertoire in the context of HIV. Gabriel is currently a researcher in Kalland's group, where he is involved in the development of cell-based therapeutic strategies for the treatment of cancer.

GAVASSO, SONIA
MS in ecology from the University of Zurich, and a PhD in clinical medicine from the University of Bergen. As a researcher in Gjertsen's group, her research focus is on rare cells in circulation, both in cancer and regenerative medicine. The project aims to accelerate knowledge on stem cell behavior and to harness immune mediated mechanisms to manipulate behavior. The methods are single cell based and aim at reliably detecting rare single cells in blood and CSF with high parameter suspension and imaging mass cytometry.

GELEBART, PASCAL
PhD in the field of immune oncology from the University of Paris, Hospital Saint-Louis Research Institute. He is currently a researcher in the McCormack group, working on the Prelim project towards the development of novel preclinical models of leukemias and lymphomas as well as identification of novel targeted and immune therapies for hematological malignancies.

GISSUM, KAREN ROSNES
MS in evidence-based practice and an oncology nurse. She is since March 2020 a PhD candidate in The Precision Oncology Research Group, with Line Bjørge as main supervisor and Roger Strand as co-supervisor. The focus of her PhD project is to reveal the association between cytoreductive surgery, inflammatory processes and patient-reported outcomes in epithelial ovarian cancer patients, and to use the knowledge obtained to identify biomarkers for disease management.

GJERDE, CHRISTIANE HELGESTAD
MD from the University of Bergen. She is now pursuing her PhD in the Bjørge and McCormack groups. Her research focuses on the development of better preclinical models of ovarian cancer, through the establishment, characterization and application of an organoid platform.

GRØNDAL, STURLA MAGNUS
MS in nanoscience from the University of Bergen and is currently a PhD candidate in the Lorens group. His PhD project is focused on how AXL signaling can lead to immune dysregulation in cancer and fibrotic diseases.

GUERREIRO, EDUARDA
MS in biomedical sciences from the University of Algarve, Portugal. She completed her PhD in June 2020 at the Institute of Oral Biology, University of Oslo, connected to the Costea group. Her PhD project was titled "Isolation and characterization of extracellular vesicles – Molecular couriers from cancer cell lines, and saliva and tear fluid from patients with primary Sjögren's syndrome," and focused on extracellular vesicles from oral cancer aiming at understanding their role in tumor progression.

GULLAKSEN, STEIN-ERIK
MS in nanotechnology and a PhD from the University of Bergen. He is currently a researcher in the Gjertsen group, where his work revolves around profiling changes in single cell immune and signal transduction in blood cells from patients with chronic myeloid leukemia enrolled in clinical trials.

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

HAJJAR, EHSAN
MS in medical cell biology from the University of Bergen and a PhD candidate in the Gjertsen group until he completed his degree in December 2020. His dissertation was titled "Next generation leukemia diagnostics and therapy through p53 isoforms" and focused on the modulation and function of p53 protein isoforms in acute myeloid leukemia, 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 the Norwegian University of Life Sciences and a PhD from the University of Bergen. 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 completed her PhD in the McCormack group in June 2020. Her research focused 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 a PhD in biomedicine from the University of Bergen, and currently a postdoc in the Gjertsen group. Her research is focused on investigating targeted therapies in acute myeloid leukemia with the aim of characterizing therapeutic effects and understanding therapy resistance mechanisms. This involves high resolution single cell analyses of clinical trial samples from AML patients treated with targeted therapies directed towards the AXL and FLT3 tyrosine kinases.

HUA, YAPING
MS in medical chemistry from Shanghai Jiaotong University, China, and a PhD candidate in the Kalland group until she completed her degree in May 2020. Her PhD project focused 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. She is currently a postdoc in the same group.

HUGDAHL, EMILIA
MD and PhD from the University of Bergen. Her PhD work was performed in the Akslen group, focusing on biomarkers for aggressive cutaneous melanoma. She is currently senior consultant at Haukeland University Hospital and a researcher in the Akslen group, focusing on markers of immune cells and angiogenesis to define subgroups of aggressive melanoma using imaging mass cytometry.

HØIVIK, ERLING
PhD in molecular biology from the University of Bergen. He is currently a researcher in the Bergen Gynecological Cancer Research Group (Krakstad group). His research is particularly focused on endometrial cancer with emphasis on metastatic spread, using genetics and genomics analysis.

INGEBRIKTSEN, LISE M.
MS in biomedicine from the University of Tromsø. She is currently a PhD candidate in the Akslen and Wik groups, with Elisabeth Wik as main supervisor. Her PhD project focuses on identifying biomarkers with clinical relevance, explaining some of the increased tumor aggressiveness seen in breast cancer of the young, with potential for improving individualized treatment and outcome.

JACOB, HAVJIN
MS in molecular medicine from NTNU and a PhD from the University of Bergen. She 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 with specialty in oncology, and a PhD from the University of Bergen on prognostic factors for local recurrence in soft tissue sarcoma. She was a postdoc in the Gjertsen group until March 2020, focusing on biomarkers in clinical trials of advanced cancer, with particular interest in liquid biopsies to evaluate tumor responsiveness during targeted therapy tailored to the tumor microenvironment and immune system. She is currently an adjunct associate professor with the same research focus.

KANG, JING
MS in dermatology and venereology from Shandong University, and another MS in biomedicine from the University of Bergen. She is since 2016 a PhD candidate in the Lorens group. Her PhD project focuses on the role of AXL signaling in cancer. The overall aim is to study TAM receptor dynamics in melanoma therapy resistance. She has explored how GAS6-mediated AXL receptor clustering activate unique cell signaling pathways underlying EMT and metastasis, and whether the role of AXL receptors in SARS-CoV-2 infection implicates bemcentinib as a potential therapeutic.

KANG, JIYEON
PharmD and MS in global health from the London School of Economics and Political Science. She is a PhD candidate in the Health Economics group at the London School of Hygiene and Tropical Medicine, supervised by John Cairns, focusing on how real-world data could be utilized in Health Technologies Assessment and especially related to targeted cancer treatments.

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

KLEFTOGIANNIS, DIMITRIOS
Diploma in computer science and engineering, with MS and a PhD in bioinformatics, focusing on computational identification of enhancers and promoters from genomic and epigenomic datasets. Currently he is a postdoc with the Jonassen and Akslen groups, where he is developing computational methods for single cell analysis, combined with machine learning algorithms to gain insights into cancer progression mechanisms.

KLEINMANNS, KATRIN
MS in biomedicine from Hannover Medical School, Germany, and a PhD in immuno-oncology from the University of Bergen. Currently she is a postdoc in the INOvA group (McCormack & Bjørge), focusing on the development of immunocompetent patient-derived xenograft models of high-grade serous ovarian cancer to improve therapeutic interventions by optimizing image-guided surgery and testing immunotherapies.

KLINGEN, TOR AUDUN
MD from Århus University, Denmark, senior consultant in pathology (Tønsberg), with a PhD from the University of Bergen. He did his PhD work in the Akslen group on vascular invasion by tumor cells and other prognostic factors in a population-based breast cancer study. He is currently a researcher in the Akslen group, focusing on immune cells and vascular biology in breast cancer. He is a co-supervisor for PhD candidate Ying Chen.

KNUTSVIK, GØRIL
MD and PhD from the University of Bergen. She did her PhD work in the Akslen group, concentrating on biomarkers in breast cancer with a special focus on tumor cell proliferation. She is currently a senior consultant in pathology at Haukeland University Hospital, and a researcher in the Akslen group, working on biomarkers of aggressive breast cancer.

LANGER, ANIKA
PhD in biomedicine from the University of Dresden, Germany. Since 2018, she is working in the PrecOS lab with the McCormack group, focusing on validation of new therapeutic approaches for pancreatic ductal adenocarcinoma (PDAC) *in vitro* and *in vivo*, and the development of innovative 3D cell culture methods to improve therapeutic efficacy in PDAC.

LEITCH, CALUM
MS in molecular and cellular biology from the University of Glasgow. He is currently 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.

LELLAHI, SEYED MOHAMMAD
MS in medical cell biology from the University of Bergen, and a PhD from the University of Tromsø. Mohammad is currently a postdoc in Kalland's group, studying whether two dendritic cell subpopulations, conventional type 1 DCs and conventional type 2 DCs, are a better alternative for moDC in cryoimmunotherapy (CryoIT) treatment. Furthermore, he will be developing an "Organoid and DC co-culture model system" to study immune cells and cancer material in a more complex environment using the Helios Hyperion Imaging System mass cytometry platform

LIEN, HILDE EIDE
MS in biomedicine from the University of Bergen on Helios CyTOF analysis of intra-tumoral immune cells in obese mice. Hilde is currently a PhD candidate in the Bergen Gynecologic Cancer Group (Krakstad) where she is using imaging mass cytometry to investigate tumor heterogeneity and prognostic molecular markers in endometrial cancer.

LOTSBERG, MARIA LIE
MS in nanoscience and a PhD from the University of Bergen, 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 currently a postdoc in Lorens' group, working on imaging mass cytometry and high dimensional analysis of the tumor microenvironment.

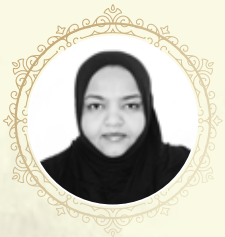
LUÍS, ANA BEATRIZ MATEUS D'AVÓ
MS in economics from the Nova School of Business and Economics, Portugal. She completed her PhD in February 2021 in the Health Economics Group of CCBIO, focused on the cost-effectiveness of biomarkers in the Norwegian healthcare system and on the incentives of pharmaceutical companies to invest in R&D of drugs with biomarkers.

LURA, NJÅL GJÆRDE
MD with background in internal medicine and radiology. He is currently 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 was a postdoc in Lorens' group from 2018 to until February 2021, where her research focused on tumor cell plasticity in malignant melanoma and its role in therapy resistance with a particular focus on AXL receptor kinase mechanisms.

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

MOHAMED, NAZAR GAFAR ABDULRAHMAN
Dentist and oral microbiologist with a BDS degree and an MS in molecular medicine from the University of Khartoum, Sudan. He was a PhD candidate in the Costea group until he completed his degree in June 2020. His PhD project was titled "Biomarker Identification in Oral Squamous Cell Carcinoma: Study on Cohorts of Patients from Sudan," and focused 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 was also exploring the validity for clinical application of an electronic nose device, as a rapid and cost-effective screening tool for oral cancer (OSSC).



MOHAMED, NUHA
MS in periodontics from the University of Khartoum. She is since August 2016 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. He is currently a PhD candidate in the Gullberg group, where his PhD project is focused on the role of integrin α11 in fibrosis and characterization of new tools for anti-fibrotic research.

NGINAMAU, ELISABETH SIVY
MD from the University of Padua (Italy) and a PhD from the University of Bergen. She is a specialist in pathology and currently a consultant at the Department of Pathology, Haukeland University Hospital and a guest researcher in the Costea group. Her research focuses on oral cancer with a special interest on the impact of immune response on oral cancer's clinical behavior and immune response regulation.

OMSLAND, MARIA
MS and PhD in medical cell biology from the University of Bergen. She is since august 2019 a postdoc in the Gjertsen group, where 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
BDS from the Tribhuvan University Nepal. He completed his PhD in 2016 on integrin α11 in oral carcinogenesis at the University of Bergen. He was a postdoc in the Thorsen Lab at UiB from 2017 to August 2019, doing research on melanoma brain metastasis. Currently he is a guest researcher in the Costea group, working on oral carcinogenesis.

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
MS in medical cell biology from the University of Bergen. He is since 2015 a PhD candidate in the Costea group. His research focuses on the identification of micro-RNA signatures in the tumor stroma that can be used as prognostic factors and for therapeutic intervention in oral squamous cell carcinoma.

RANE, LALIT SHIRISH
DVM from India and an MS in molecular biology. He gained his PhD in 2014 on immunology and IL-7 isoforms at the Karolinska Institute, Sweden. He started working with the Gjertsen group as a postdoc in 2015, investigating p53 isoforms in AML. Currently he is a researcher in the same group, investigating novel small molecule CSF1R and FLT3 inhibitors in AML.

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

RAYFORD, AUSTIN JAMES
MS in biomedical sciences from the University of Bergen. He is currently pursuing a joint industrial PhD with the Lorens group and BerGenBio, where he plays a key role in identifying clinical and translational biomarkers in a majority of BerGenBio's clinical trials of AXL-inhibitors, with an emphasis on highly multiplexed datasets and development of imaging mass cytometry-based approaches.

RANA, NEHA
MS in biochemistry from India. She is since 2018 a PhD candidate in the Mustafa and Gjertsen groups, where her project explores immune interactions in mesenchymal stem cell based regenerative therapies with special focus on liquid biopsy approaches.

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

SCHUSTER, CORNELIA
MD and Dr. Med from the Friedrich-Alexander University of Erlangen, Nurnberg, Germany. She gained her PhD on predictive markers in metastatic melanoma in 2016 at 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 the Norwegian University of Science and Technology. 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 the London School of Economics and the London School of Hygiene and Tropical Medicine (LSHTM). She completed her PhD in health economics in November 2020, as part of the Health Economics group of CCBIO, focusing on economic evaluations of cancer biomarkers under the supervision of John Cairns at LSHTM. Kelly is now a postdoc at the Imperial College London.

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

SMELAND, HILDE YTRE-HAUGE
MD from the University of Bergen. She is currently a PhD candidate in the Akslen group and Linda Stuhr is her main supervisor. 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 and a PhD from the University of Bergen. She is a postdoc in the Costea group since February 2017, focusing 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 and Wik groups, with Elisabeth Wik as main supervisor. Her project is focused on hormone receptor regulators and immune responses in primary and metastatic breast cancer.

TISLEVOLL, BENEDICTE SJO
MD from the University of Bergen. She is currently a PhD candidate in the Gjertsen group, where her project is focused on early therapy response evaluation in acute myeloid leukemia, using Mass Cytometry (CyTOF) to investigate signaling events in immune-phenotypical cell clusters to separate responders from non-responders.

TANDARIĆ, LUKA
MS in molecular biology from the University of Zagreb, Croatia. He joined the INOvA group in 2020 as a PhD candidate, with Line Bjørge and Emmet McCormack as main supervisors. His project aims to describe the value of combined CD73 and PD-L1 blockade in patients with relapsed high-grade serous ovarian cancer.

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

THOMSEN, LIV CECILIE VESTRHEIM
MD and specialist in obstetrics and gynecology. She completed her PhD in 2015 at the University of Bergen, focusing on the genetic background of complex diseases. She currently holds a researcher position in the Gjertsen group, with main focus on mass cytometry (CyTOF) analyses, to develop antibody panels for immune cells and checkpoint inhibitor responses in patient-derived materials. Thomsen also works on analyses of data from early phase clinical trials on prostate and ovarian cancer.

TORNAAS, STIAN
MS in biomedicine from the University of Tromsø. He is currently a PhD candidate in the Costea group, where his work aims to identify different CAF phenotypes in HNSCC by using Hyperion imaging mass cytometry, studying their role in resistance to therapy using cohorts of patient tissue.

TRANVÅG, EIRIK JOAKIM
MD from the University of Bergen. He is 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 contribute towards better and fairer priority setting, and in particular how the personalization of cancer medicine can alter priority setting practice. His broader research interests 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 from the University of Bergen on stem cells research and diabetes. She is currently a postdoc in the Akslen group. Vethe's research is focused 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, immunohistochemistry, and cell models.

VIÑEGRA, ELVIRA GARCÍA DE JALÓN
MS in organic synthesis and medicinal chemistry from the University of Bergen. She is now pursuing her PhD in the McCormack group, focused 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
Oncology nurse who holds an MS and is since March 2020 a PhD candidate in the Bergen Gynecologic Cancer Research Group with Camilla Krakstad. In her PhD project, she is working on advanced MRI for developing more personalized treatment strategies in uterine cervical cancer.

XENAKI, VICTORIA
DDS from the I.M. Sechenov First Moscow State Medical University. She is since 2016 a PhD candidate in the Costea group, where her project focuses on nanotechnology in dentistry, aiming to evaluate the attitude of dental health care workers towards using nanotechnology and assessing toxicity of nanoparticles used in dentistry in the context of nano-safety.

ÅSE, HILDEGUNN SIV
MD and a radiologist who also holds an MS in health economics from the University of Bergen. She is currently a PhD candidate in the Bergen Gynecologic Cancer Group with Camilla Krakstad. 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.

List of publications 2020

CCBIO - LIST OF PUBLICATIONS 2020

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

Smeland HY, Askeland C, Wik E, Knutsvik G, Molven A, Edelmann RJ, Reed RK, Warren DJ, Gullberg D, Stuhr L, Akslen LA. Integrin α11β1 is expressed in breast cancer stroma and associates with aggressive tumor phenotypes. *J Pathol Clin Res*. 2020 Jan;6(1):69-82. doi: 10.1002/cjp2.148. Epub 2019 Dec 3.

Dongre H, Rana N, Fromreide S, Rajthala S, Bøe Engelsen I, Paradis J, Gutkind JS, Vintermyr OK, Johannessen AC, Bjørge L, Costea DE. Establishment of a novel cancer cell line derived from vulvar carcinoma associated with lichen sclerosus exhibiting a fibroblast-dependent tumorigenic potential. *Exp Cell Res*. 2020 Jan 1;386(1):111684. doi: 10.1016/j.yexcr.2019.111684. Epub 2019 Oct 23.

Ray-Coquard I, Cibula D, Mirza MR, ... and AGO Study Group-led GCIG/ENGOT Intergroup Consortium, (incl. Bjørge L.) Final results from GCIG/ENGOT/AGO-OVAR 12, a randomised placebo-controlled phase III trial of nintedanib combined with chemotherapy for newly diagnosed advanced ovarian cancer. *Int J Cancer*. 2020 Jan 15;146(2):439-448. doi: 10.1002/ijc.32606. Epub 2019 Sep 6. Clinical Trial.

Izzi V, Heljasvaara R, Heikkinen A, Karppinen SM, Koivunen J, Pihlajaniemi T. Exploring the roles of MACIT and multiplexin collagens in stem cells and cancer. *Semin Cancer Biol* 62:134-148, 2020. doi: 10.1016/j.semcancer.2019.08.033.

Askeland C, Wik E, Finne K, Birkeland E, Arnes JB, Collett K, Knutsvik G, Krüger K, Davidsen B, Aas T, Eide GE, Stefansson IM, Foulkes WD, Akslen LA. Stathmin expression associates with vascular and immune responses in aggressive breast cancer subgroups. *Sci Rep*. 2020 Feb 19;10(1):2914. doi: 10.1038/s41598-020-59728-3.

Bjånes T, Kotopoulis S, Murvold ET, Kamčeva T, Gjertsen BT, Gilja OH, Schjøtt J, Riedel B, McCormack E. Ultrasound- and Microbubble-Assisted Gemcitabine Delivery to Pancreatic Cancer Cells. *Pharmaceutics*. 2020 Feb 7;12(2):141. doi: 10.3390/pharmaceutics12020141.

Fonnes T, Strand E, Fasmer KE, Berg HF, Espedal H, Sortland K, Stefansson I, Bjørge L, Haldorsen IS, Krakstad C, McCormack E. Near-Infrared Fluorescent Imaging for Monitoring of Treatment Response in Endometrial Carcinoma Patient-Derived Xenograft Models. *Cancers (Basel)*. 2020 Feb 6;12(2):370. doi: 10.3390/cancers12020370.

Xenaki V, Marthinussen MC, Costea DE, Didilescu AC, Susin C, Cimpan MR, Åstrøm AN. Knowledge about nanotechnology and intention to use nanomaterials: A comparative study among dental students in Norway and Romania. *Eur J Dent Educ*. 2020 Feb;24(1):79-87. doi: 10.1111/eje.12470. Epub 2019 Oct 16.

Forsse D, Tangen IL, Fasmer KE, Halle MK, Viste K, Almås B, Bertelsen BE, Trovik J, Haldorsen IS, Krakstad C. Blood steroid levels predict survival in endometrial cancer and reflect tumor estrogen signaling. *Gynecol Oncol*. 2020 Feb;156(2):400-406. doi: 10.1016/j.ygyno.2019.11.123. Epub 2019 Dec 6.

Klæstad E, Opdahl S, Engstrøm MJ, Ytterhus B, Wik E, Bofin AM, Valla M. MRPS23 amplification and gene expression in breast cancer; association with proliferation and the non-basal subtypes. *Breast Cancer Res Treat*. 2020 Feb;180(1):73-86. doi: 10.1007/s10549-020-05532-6. Epub 2020 Jan 16.

Webb M, Manley K, Olivan M, Guldvik I, Palczynska M, Hurst R, Connell SP, Mills IG, Brewer DS, Mills R, Cooper CS, Clark J. Methodology for the at-home collection of urine samples for prostate cancer detection. *Biotechniques*. 2020;68(2):65-71. doi.org/10.2144/btn-2019-0092.

Tsuruda KM, Hofvind S, Akslen LA, Hoff SR, Veierød MB. Terminal digit preference: a source of measurement error in breast cancer diameter reporting. *Acta Oncol*. 2020 Mar;59(3):260-267. doi: 10.1080/0284186X.2019.1669817. Epub 2019 Sep 30.

Lerche M, Elosegui-Artola A, Kechagia JZ, Guzmán C, Georgiadou M, Andreu I, Gullberg D, Roca-Cusachs P, Peuhu E, Ivaska J. Integrin Binding Dynamics Modulate Ligand-Specific Mechanosensing in Mammary Gland Fibroblasts. *iScience.* 2020 Mar 27;23(3):100907. doi: 10.1016/j.isci.2020.100907. Epub 2020 Feb 13.

Aasebø E, Berven FS, Bartaula-Brevik S, Stokowy T, Hovland R, Vaudel M, Døskeland SO, McCormack E, Batth TS, Olsen JV, Bruserud Ø, Selheim F, Hernandez-Valladares M. Proteome and Phosphoproteome Changes Associated with Prognosis in Acute Myeloid Leukemia. *Cancers (Basel).* 2020 Mar 17;12(3):709. doi: 10.3390/cancers12030709.

Omsland M, Andresen V, Gullaksen SE, Ayuda-Durán P, Popa M, Hovland R, Brendehaug A, Enserink J, McCormack E, Gjertsen BT. Tyrosine kinase inhibitors and interferon-α increase tunneling nanotube (TNT) formation and cell adhesion in chronic myeloid leukemia (CML) cell lines. *FASEB J.* 2020 Mar;34(3):3773-3791. doi: 10.1096/fj.201802061RR. Epub 2020 Jan 16.

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.

Kuusanmäki H, Leppä AM, Pölönen P, Kontro M, Dufva O, Deb D, Yadav B, Brück O, Kumar A, Everaus H, Gjertsen BT, Heinäniemi M, Porkka K, Mustjoki S, Heckman CA. Phenotype-based drug screening reveals association between venetoclax response and differentiation stage in acute myeloid leukemia. *Haematologica.* 2020 Mar;105(3):708-720. doi: 10.3324/haematol.2018.214882. Epub 2019 Jul 11.

Azeem W, Bakke RM, Appel S, Øyan AM, Kalland KH. Dual Pro- and Anti-Inflammatory Features of Monocyte-Derived Dendritic Cells. *Front Immunol.* 2020 Mar 27;11:438. doi: 10.3389/fimmu.2020.00438. eCollection 2020.

Xenaki V, Costea DE, Marthinussen MC, Cimpan MR, Åstrøm AN. Use of nanomaterials in dentistry: covariates of risk and benefit perceptions among dentists and dental hygienists in Norway. *Acta Odontol Scand.* 2020 Mar;78(2):152-160. doi: 10.1080/00016357.2019.1668055. Epub 2019 Sep 27.

Zhang Z, Gao Z, Rajthala S, Sapkota D, Dongre H, Parajuli H, Suliman S, Das R, Li L, Bindoff LA, Costea DE, Liang X. Metabolic reprogramming of normal oral fibroblasts correlated with increased glycolytic metabolism of oral squamous cell carcinoma and precedes their activation into carcinoma associated fibroblasts. *Cell Mol Life Sci.* 2020 Mar;77(6):1115-1133. doi: 10.1007/s00018-019-03209-y. Epub 2019 Jul 3.

Berg HF, Ju Z, Myrvold M, Fasmer KE, Halle MK, Hoivik EA, Westin SN, Trovik J, Haldorsen IS, Mills GB, Krakstad C, Werner HMJ. Development of prediction models for lymph node metastasis in endometrioid endometrial carcinoma. *Br J Cancer.* 2020 Mar;122(7):1014-1022. doi: 10.1038/s41416-020-0745-6. Epub 2020 Feb 10.

Lazarian G, Friedrich C, Quinquenel A, … and Baran-Marszak F., (incl. McCormack E.) Stabilization of β-catenin upon B-cell receptor signaling promotes NF-kB target genes transcription in mantle cell lymphoma. *Oncogene.* 2020 Apr;39(14):2934-2947. doi: 10.1038/s41388-020-1183-x. Epub 2020 Feb 7.

Vistad I, Bjørge L, Skeie-Jensen T. Need for change in cancer follow-up. *Tidsskr Nor Laegeforen.* 2020 Apr 20;140. doi: 10.4045/tidsskr.20.0281. Print 2020 Apr 21.

Engerud H, Berg HF, Myrvold M, Halle MK, Bjorge L, Haldorsen IS, Hoivik EA, Trovik J, Krakstad C. High degree of heterogeneity of PD-L1 and PD-1 from primary to metastatic endometrial cancer. *Gynecol Oncol.* 2020 Apr;157(1):260-267. doi: 10.1016/j.ygyno.2020.01.020. Epub 2020 Jan 21.

Landi MT, Bishop DT, MacGregor S, ... Law MH, (incl. Akslen LA.) Genome-wide association meta-analyses combining multiple risk phenotypes provide insights into the genetic architecture of cutaneous melanoma susceptibility. *Nat Genet.* 2020 May;52(5):494-504. doi: 10.1038/s41588-020-0611-8. Epub 2020 Apr 27.

Zeltz C, Primac I, Erusappan P, Alam J, Noel A, Gullberg D. Cancer-associated fibroblasts in desmoplastic tumors: emerging role of integrins. *Semin Cancer Biol.* 2020 May;62:166-181. doi: 10.1016/j.semcancer.2019.08.004. Epub 2019 Aug 12.

Chouaib S, Lorens J. Editorial: Targeting the Tumor Microenvironment for a More Effective and Efficient Cancer Immunotherapy. *Front Immunol.* 2020 May 15;11:933. doi: 10.3389/fimmu.2020.00933. eCollection 2020.

Mercatelli D, Bortolotti M, Andresen V, Sulen A, Polito L, Gjertsen BT, Bolognesi A. Early Response to the Plant Toxin Stenodactylin in Acute Myeloid Leukemia Cells Involves Inflammatory and Apoptotic Signaling. *Front Pharmacol.* 2020 May 8;11:630. doi: 10.3389/fphar.2020.00630. eCollection 2020.

Bjørsvik HR, Gjertsen BT, Elumalai V. Hit to Leads with Cytotoxic Effect in Leukemic Cells: Total Synthesis Intermediates as a Molecule Treasure Chest. *ChemMedChem.* 2020 May 19;15(10):862-870. doi: 10.1002/cmdc.202000066. Epub 2020 Apr 21.

Pandey S, Follin-Arbelet B, Pun CB, Gautam DK, Johannessen AC, Petersen FC, Costea DE, Sapkota D. Helicobacter pylori was not detected in oral squamous cell carcinomas from cohorts of Norwegian and Nepalese patients. *Sci Rep.* 2020 May 26;10(1):8737. doi: 10.1038/s41598-020-65694-7.

Reijnen C, Gogou E, Visser NCM, ... and Pijnenborg JMA, (incl. Krakstad C, Amant F.) Preoperative risk stratification in endometrial cancer (ENDORISK) by a Bayesian network model: A development and validation study. *PLoS Med.* 2020 May 15;17(5):e1003111. doi: 10.1371/journal.pmed.1003111. eCollection 2020 May.

Sivertsen Åsrud K, Bjørnstad R, Kopperud R, Pedersen L, van der Hoeven B, Karlsen TV, Brekke Rygh C, Curry FR, Bakke M, Reed RK, Tenstad O, Døskeland SO. Epac1 null mice have nephrogenic diabetes insipidus with deficient corticopapillary osmotic gradient and weaker collecting duct tight junctions. *Acta Physiol (Oxf).* 2020 May;229(1):e13442. doi: 10.1111/apha.13442. Epub 2020 Feb 3.

Fasmer KE, Gulati A, Dybvik JA, Ytre-Hauge S, Salvesen Ø, Trovik J, Krakstad C, Haldorsen IS. Preoperative 18F-FDG PET/CT tumor markers outperform MRI-based markers for the prediction of lymph node metastases in primary endometrial cancer. *Eur Radiol.* 2020 May;30(5):2443-2453. doi: 10.1007/s00330-019-06622-w. Epub 2020 Feb 7.

Kleinmanns K, Bischof K, Anandan S, Popa M, Akslen LA, Fosse V, Karlsen IT, Gjertsen BT, Bjørge L, McCormack E. CD24-targeted fluorescence imaging in patient-derived xenograft models of high-grade serous ovarian carcinoma. *EBioMedicine.* 2020 Jun;56:102782. doi: 10.1016/j.ebiom.2020.102782. Epub 2020 May 23.

Lotsberg ML, Wnuk-Lipinska K, Terry S, … and Engelsen AST, (incl. Brekken RA, Akslen LA, Thiery JP, Lorens JB.) AXL Targeting Abrogates Autophagic Flux and Induces Immunogenic Cell Death in Drug-Resistant Cancer Cells. *J Thorac Oncol.* 2020 Jun;15(6):973-999. doi: 10.1016/j.jtho.2020.01.015. Epub 2020 Feb 1.

Kleinmanns K, Fosse V, Davidson B, de Jalón EG, Tenstad O, Bjørge L, McCormack E. CD24-targeted intraoperative fluorescence image-guided surgery leads to improved cytoreduction of ovarian cancer in a preclinical orthotopic surgical model. *EBioMedicine.* 2020 Jun;56:102783. doi: 10.1016/j.ebiom.2020.102783. Epub 2020 May 23.

Majumder MM, Leppä AM, Hellesøy M, Dowling P, Malyutina A, Kopperud R, Bazou D, Andersson E, Parsons A, Tang J, Kallioniemi O, Mustjoki S, O'Gorman P, Wennerberg K, Porkka K, Gjertsen BT, Heckman CA. Multi-parametric single cell evaluation defines distinct drug responses in healthy hematologic cells that are retained in corresponding malignant cell types. *Haematologica.* 2020 Jun;105(6):1527-1538. doi: 10.3324/haematol.2019.217414. Epub 2019 Aug 22.

Hesjedal MB, Åm H, Sørensen KH, Strand R. Transforming Scientists' Understanding of Science-Society Relations. Stimulating Double-Loop Learning when Teaching RRI. *Sci Eng Ethics*. 2020 Jun;26(3):1633-1653. doi: 10.1007/s11948-020-00208-2. Epub 2020 Mar 16.

Gierman LM, Silva GB, Pervaiz Z, Rakner JJ, Mundal SB, Thaning AJ, Nervik I, Elschot M, Mathew S, Thomsen LCV, Bjørge L, Iversen AC. TLR3 expression by maternal and fetal cells at the maternal-fetal interface in normal and preeclamptic pregnancies. *J Leukoc Biol*. 2020 Jun 23. doi: 10.1002/JLB.3MA0620-728RR. Online ahead of print.

Maynou L, Cairns J. Disagreement on cancer drug decisions in Europe. *Int J Technol Assess Health Care*. 2020 Jun;36(3):232-238. doi: 10.1017/S026646232000032X. Epub 2020 Jun 15.

Gajurel R, Gautam DK, Pun CB, Dhakal HP, Petrovski BÉ, Costea DE, Sapkota D. Trends and clinicopathological characteristics of oral squamous cell carcinomas reported at a tertiary cancer hospital in Nepal during 1999 to 2009. *Clin Exp Dent Res*. 2020 Jun;6(3):356-362. doi: 10.1002/cre2.278. Epub 2020 Jan 12.

Petäistö T, Vicente D, Mäkelä KA, Finnilä MA, Miinalainen I, Koivunen J, Izzi V, Aikio M, Karppinen SM, Devarajan R, Herzig KH, Heljasvaara R, Pihlajaniemi T. Lack of collagen XVIII leads to lipodystrophy and perturbs hepatic glucose and lipid homeostasis. *J Physiol* 598(16):3373-3393,2020. doi: 10.1113/JP279559.

Huynh-Le MP, Fan CC, Karunamuni R,... and Consortium P, (incl. Mills IG.) A Genetic Risk Score to Personalize Prostate Cancer Screening, Applied to Population Data. *Cancer Epidemiol Biomarkers Prev*. 2020;29(9):1731-8.

Karunamuni RA, Huynh-Le MP, Fan CC, ... and Consortium P, (incl. Mills IG.) The effect of sample size on polygenic hazard models for prostate cancer. *Eur J Hum Genet*. 2020;28(10):1467-75.

Bergholtz H, Lien TG, Swanson DM, Frigessi A; Oslo Breast Cancer Research Consortium (OSBREAC), Daidone MG, Tost J, Wärnberg F, Sørlie T. Contrasting DCIS and invasive breast cancer by subtype suggests basal-like DCIS as distinct lesions. *NPJ Breast Cancer*. 2020 Jun 17;6:26. doi: 10.1038/s41523-020-0167-x. eCollection 2020.

Lofterød T, Frydenberg H, Flote V, Eggen AE, McTiernan A, Mortensen ES, Akslen LA, Reitan JB, Wilsgaard T, Thune I. Exploring the effects of lifestyle on breast cancer risk, age at diagnosis, and survival: the EBBA-Life study. *Breast Cancer Res Treat*. 2020 Jul;182(1):215-227. doi: 10.1007/s10549-020-05679-2. Epub 2020 May 20.

Ossenkoppele GJ, Breems DA, Stuessi G, ... and SAKK, (incl. Gjertsen B.) Lenalidomide added to standard intensive treatment for older patients with AML and high-risk MDS. *Leukemia*. 2020 Jul;34(7):1751-1759. doi: 10.1038/s41375-020-0725-0. Epub 2020 Feb 4. Clinical Trial.

Obermair A, Baxter E, Brennan DJ, McAlpine JN, Muellerer JJ, Amant F, van Gent MDJM, Coleman RL, Westin SN, Yates MS, Krakstad C, Janda M. Fertility-sparing treatment in early endometrial cancer: current state and future strategies. *Obstet Gynecol Sci*. 2020 Jul;63(4):417-431. doi: 10.5468/ogs.19169. Epub 2020 Jul 8.

Fresques TM and LaBarge MA. Contributions of YAP and TAZ dysfunction to breast cancer initiation, progression, and aging-related susceptibility. *Aging and Cancer* (2020) 03 July. doi.org/10.1002/aac2.12011.

Hochhaus A, Gambacorti-Passerini C, Abboud C, Gjertsen BT, Brümmendorf TH, Smith BD, Ernst T, Giraldo-Castellano P, Olsson-Strömberg U, Saussele S, Bardy-Bouxin N, Viqueira A, Leip E, Russell-Smith TA, Leone J, Rosti G, Watts J, Giles FJ; BYOND Study Investigators. Bosutinib for pretreated patients with chronic phase chronic myeloid leukemia: primary results of the phase 4 BYOND study. *Leukemia*. 2020 Aug;34(8):2125-2137. doi: 10.1038/s41375-020-0915-9. Epub 2020 Jun 22. Clinical Trial.

Alme E, Törnroos KW, Gjertsen BT, Bjørsvik HR. Synthesis of N-Aryl- and N-alkyl-Substituted Imidazolium Silver Complexes: Cytotoxic Screening by Using Human Cell Lines Modelling Acute Myeloid Leukaemia. *ChemMedChem*. 2020 Aug 19;15(16):1509-1514. doi: 10.1002/cmdc.202000138. Epub 2020 Jul 9.

Pandey S, Osman TA, Sharma S, Vallenari EM, Shahdadfar A, Pun CB, Gautam DK, Uhlin-Hansen L, Rikardsen O, Johannessen AC, Costea DE, Sapkota D. Loss of S100A14 expression at the tumor-invading front correlates with poor differentiation and worse prognosis in oral squamous cell carcinoma. *Head Neck*. 2020 Aug;42(8):2088-2098. doi: 10.1002/hed.26140. Epub 2020 Mar 23.

Steigen SE, Søland TM, Nginamau ES, Laurvik H, Costea DE, Johannessen AC, Jebsen P, Bjerkli IH, Uhlin-Hansen L, Hadler-Olsen E. Grading of oral squamous cell carcinomas - Intra and interrater agreeability: Simpler is better? *J Oral Pathol Med.* 2020 Aug;49(7):630-635. doi: 10.1111/jop.12990. Epub 2020 Jan 19.

Seo MK, Straume O, Akslen LA, Cairns J. HSP27 Expression as a Novel Predictive Biomarker for Bevacizumab: is it Cost Effective? *Pharmacoecon Open*. 2020 Sep;4(3):529-539. doi: 10.1007/s41669-019-00193-8.

Koivunen J, Tu H, Kemppainen A, Anbazhagan P, Finnilä MA, Saarakkala S, Käpylä J, Lu N, Heikkinen A, Juffer AH, Heino J, Gullberg D, Pihlajaniemi T. Integrin α11β1 is a receptor for collagen XIII. (Erratum.) *Cell Tissue Res.* 2020 Dec 11. doi: 10.1007/s00441-020-03300-y. Online ahead of print.

Bae CA, Ham IH, Oh HJ, Lee D, Woo J, Son SY, Yoon JH, Lorens JB, Brekken RA, Kim TM, Han SU, Park WS, Hur H. Inhibiting the GAS6/AXL axis suppresses tumor progression by blocking the interaction between cancer-associated fibroblasts and cancer cells in gastric carcinoma. *Gastric Cancer*. 2020 Sep;23(5):824-836. doi: 10.1007/s10120-020-01066-4. Epub 2020 Apr 2.

Wang X, Deng L, Gjertsen BT. A microfluidic device for differential capture of heterogeneous rare tumor cells with epithelial and mesenchymal phenotypes. *Anal Chim Acta.* 2020 Sep 8;1129:1-11. doi: 10.1016/j.aca.2020.06.060. Epub 2020 Jul 19.

Guerreiro EM, Øvstebø R, Thiede B, Costea DE, Søland TM, Kanli Galtung H. Cancer cell line-specific protein profiles in extracellular vesicles identified by proteomics. *PLoS One*. 2020 Sep 4;15(9):e0238591. doi: 10.1371/journal.pone.0238591. eCollection 2020.

García-Ponce A, Schuster K, Døskeland SO, Reed RK, Curry FE, Waschke J, Radeva MY. Epac1 Is Crucial for Maintenance of Endothelial Barrier Function through A Mechanism Partly Independent of Rac1. *Cells*. 2020 Sep 25;9(10):2170. doi: 10.3390/cells9102170.

Karunamuni RA, Huynh-Le MP, Fan CC, ... and Consortium P, (incl. Mills IG.) African-specific improvement of a polygenic hazard score for age at diagnosis of prostate cancer. *Int J Cancer*. 2021 Jan 1;148(1):99-105. doi: 10.1002/ijc.33282. Epub 2020 Sep 24.

Engelsen AST, Wnuk-Lipinska K, Bougnaud S, … and Lorens JB, (incl. Sørlie T, Brekken RA, Straume O, Thiery JP, Akslen LA, LaBarge MA.) AXL Is a Driver of Stemness in Normal Mammary Gland and Breast Cancer. *iScience.* 2020 Oct 7;23(11):101649. doi: 10.1016/j.isci.2020.101649. eCollection 2020 Nov 20.

Ossenkoppele GJ, Breems DA, Stuessi G, ... and SAKK (incl. Gjertsen B.) Correction: Lenalidomide added to standard intensive treatment for older patients with AML and high-risk MDS. *Leukemia*. 2020 Oct;34(10):2820. doi: 10.1038/s41375-020-0994-7.

Silva GB, Gierman LM, Rakner JJ, Stødle GS, Mundal SB, Thaning AJ, Sporsheim B, Elschot M, Collett K, Bjørge L, Aune MH, Thomsen LCV, Iversen AC. Cholesterol Crystals and NLRP3 Mediated Inflammation in the Uterine Wall Decidua in Normal and Preeclamptic Pregnancies. *Front Immunol*. 2020 Oct 8;11:564712. doi: 10.3389/fimmu.2020.564712. eCollection 2020.

Guldvik IJ, Zuber V, Braadland PR, Grytli HH, Ramberg H, Lilleby W, Thiede B, Zucknick M, Saatcioglu F, Gislefoss R, Kvåle R, George A, Grönberg H, Wiklund F, Neal DE, Gnanapragasam VJ, Taskén KA, Mills IG. Identification and Validation of Leucine-rich α-2-glycoprotein 1 as a Noninvasive Biomarker for Improved Precision in Prostate Cancer Risk Stratification. *European Urology Open Science*. 2020;21:51-60.

Kleinmanns K, Fosse V, Bjørge L, McCormack E. The Emerging Role of CD24 in Cancer Theranostics-A Novel Target for Fluorescence Image-Guided Surgery in Ovarian Cancer and Beyond. *J Pers Med*. 2020 Nov 27;10(4):255. doi: 10.3390/jpm10040255. Review.

Haugse R, Langer A, Murvold ET, Costea DE, Gjertsen BT, Gilja OH, Kotopoulis S, Ruiz de Garibay G, McCormack E. Low-Intensity Sonoporation-Induced Intracellular Signalling of Pancreatic Cancer Cells, Fibroblasts and Endothelial Cells. *Pharmaceutics*. 2020 Nov 6;12(11):1058. doi: 10.3390/pharmaceutics12111058.

Nené NR, Barrett J, Jones A, Evans I, Reisel D, Timms JF, Paprotka T, Leimbach A, Franchi D, Colombo N, Bjørge L, Zikan M, Cibula D, Widschwendter M. DNA methylation signatures to predict the cervicovaginal microbiome status. *Clin Epigenetics*. 2020 Nov 23;12(1):180. doi: 10.1186/s13148-020-00966-7.

Fasmer KE, Hodneland E, Dybvik JA, Wagner-Larsen K, Trovik J, Salvesen Ø, Krakstad C, Haldorsen IHS. Whole-Volume Tumor MRI Radiomics for Prognostic Modeling in Endometrial Cancer. *J Magn Reson Imaging*. 2020 Nov 16. doi: 10.1002/jmri.27444. Online ahead of print.

Baxter E, Brennan DJ, McAlpine JN, Mueller JJ, Amant F, van Gent MDJM, Huntsman DG, Coleman RL, Westin SN, Yates MS, Krakstad C, Quinn MA, Janda M, Obermair A. Improving response to progestin treatment of low-grade endometrial cancer. *Int J Gynecol Cancer.* 2020 Nov;30(11):1811-1823. doi: 10.1136/ijgc-2020-001309. Epub 2020 May 6. Review.

Jokela TA, LaBarge MA. Integration of Mechanical and ECM Microenvironment Signals in the Determination of Cancer Stem Cell States. *Current Stem Cell Reports* (2020). doi. org/10.1007/s40778-020-00182-2.

Koivunen J, Tu H, Kemppainen A, Anbazhagan P, Finnilä MA, Saarakkala S, Käpylä J, Lu N, Heikkinen A, Juffer AH, Heino J, Gullberg D, Pihlajaniemi T. Integrin α11β1 is a receptor for collagen XIII. *Cell Tissue Res.* 2020 Dec 11. doi: 10.1007/s00441-020-03300-y. Online ahead of print.

Fagerholt OHE, Hellesøy M, Gullaksen SE, Gjertsen BT. Single Cell Detection of the p53 Protein by Mass Cytometry. *Cancers (Basel).* 2020 Dec 9;12(12):3699. doi: 10.3390/cancers12123699.

Tadele DS, Robertson J, Crispin R, Herrera MC, Chlubnova M, Piechaczyk L, Ayuda-Durán P, Singh SK, Gedde-Dahl T, Floisand Y, Skavland J, Wesche J, Gjertsen BT, Enserink JM. A cell competition-based small molecule screen identifies a novel compound that induces dual c-Myc depletion and p53 activation. *J Biol Chem.* 2020 Dec 10:jbc.RA120.015285. doi: 10.1074/jbc.RA120.015285. Online ahead of print.

Onyango TB, Hjelle SM, Haaland I, Vintermyr OK, Johannessen AC, Gjertsen BT. A Comparison of p53 Isoform Profiles and Apoptosis Induced by Camptothecin or a Herbal Khat Extract (Catha Edulis (Vahl) Forssk. ex Endl.) in Leukemic Cell Lines: Exploring Cellular Responses in Therapy Development. *Cancers (Basel).* 2020 Dec 1;12(12):3596. doi: 10.3390/cancers12123596.

Tambe M, Karjalainen E, Vähä-Koskela M, Bulanova D, Gjertsen BT, Kontro M, Porkka K, Heckman CA, Wennerberg K. Pan-RAF inhibition induces apoptosis in acute myeloid leukemia cells and synergizes with BCL2 inhibition. *Leukemia.* 2020 Dec;34(12):3186-3196. doi: 10.1038/s41375-020-0972-0. Epub 2020 Jul 10.

Bjerkli IH, Hadler-Olsen E, Nginamau ES, Laurvik H, Søland TM, Costea DE, Uhlin-Hansen L, Steigen SE. A combined histo-score based on tumor differentiation and lymphocytic infiltrate is a robust prognostic marker for mobile tongue cancer. *Virchows Arch*. 2020 Dec;477(6):865-872. doi: 10.1007/s00428-020-02875-9. Epub 2020 Jun 30.

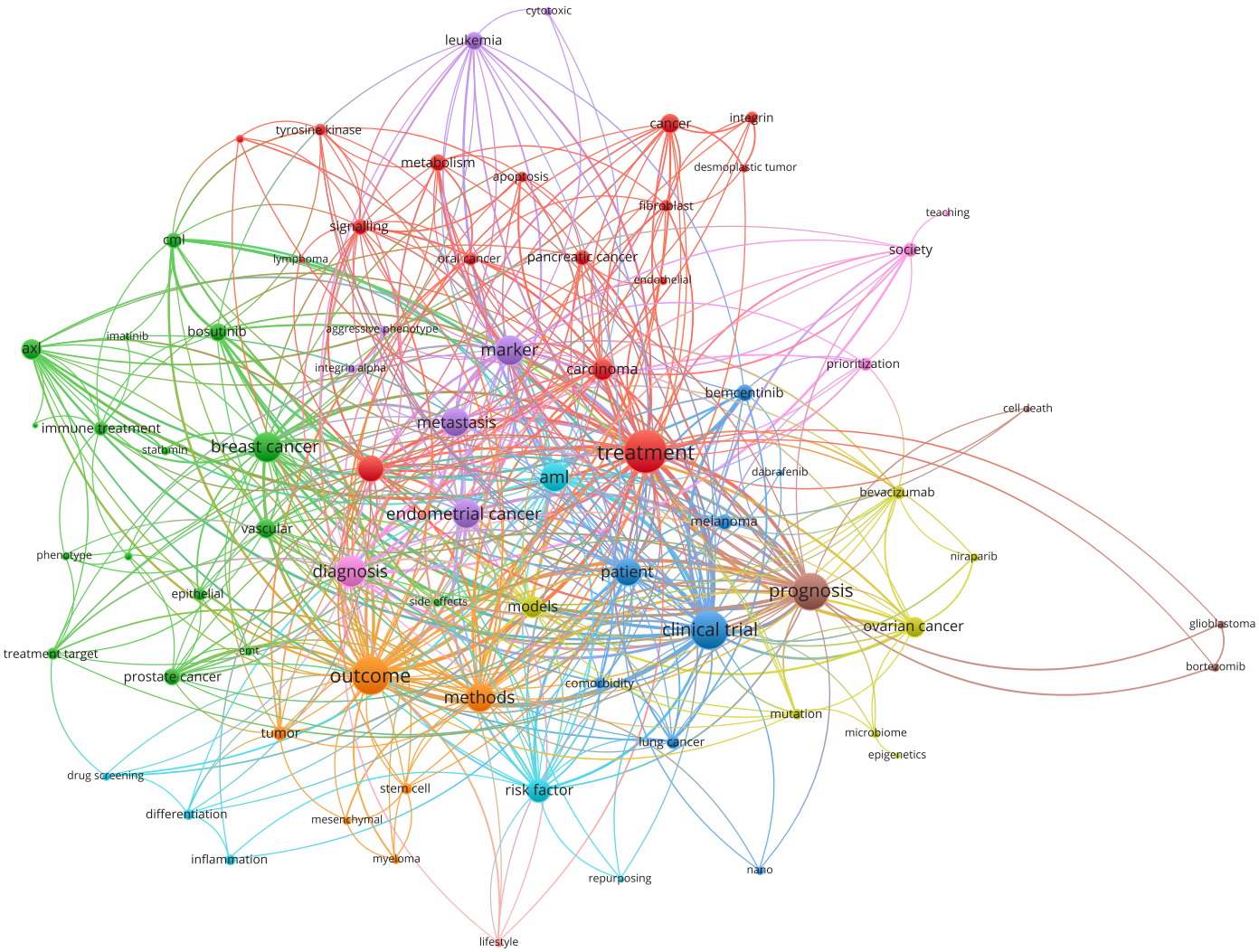
van Weelden WJ, Reijnen C, Küsters-Vandevelde HVN, ... and ENITEC-Consortium, (incl. Amant F, Krakstad C.) The cutoff for estrogen and progesterone receptor expression in endometrial cancer revisited: a European Network for Individualized Treatment of Endometrial Cancer collaboration study. *Hum Pathol.* 2020 Dec 15;109:80-91. doi: 10.1016/j.humpath.2020.12.003. Online ahead of print.

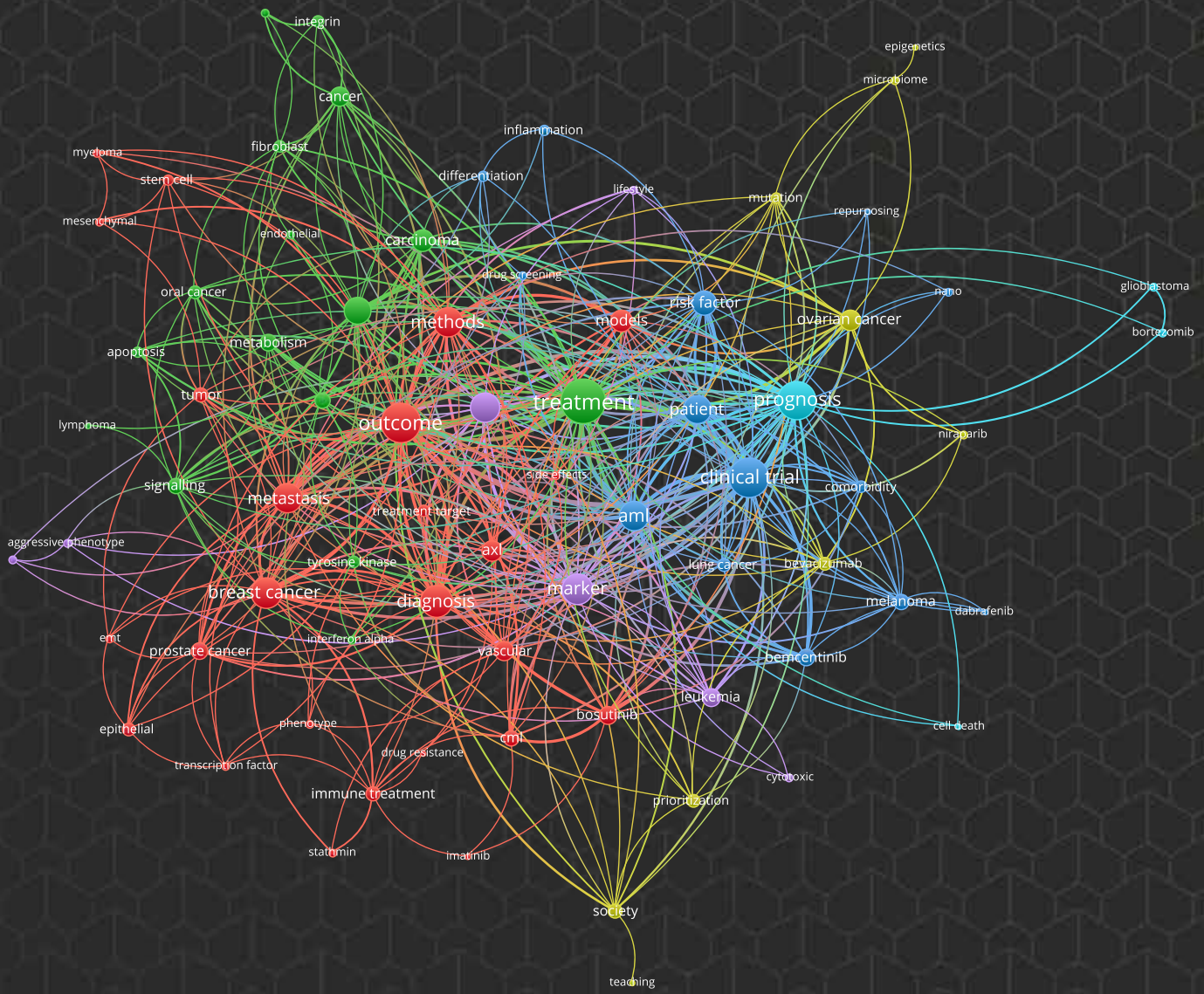
Jokela TA, Todhunter ME, and LaBarge MA (2020). High-throughput microenvironment microarray (MEMA) high-resolution imaging. Bioengineering Technologies. Edited by Rasooly, Ossandon, and Baker. *Springer Publishing*.

Eds. Strauss B, Bertolaso M, Ernberg I, Bissel MJ. Rethinking Cancer; A New Paradigm for the Postgenomics Era. *From Vienna Series in Theoretical Biology, MIT Press*. ISBN: 9780262045216.

CCBIO BIBLIOGRAPHICS

The figures reflect a bibliometric analysis of terms used in the titles of CCBIOs scientific publications during 2019-2020. The thickness of the lines illustrates the strength of relations between terms, and the size of the dots illustrate the frequency of the terms used. The two figures illustrate alternative views.

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drug screening
oral cancer
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risk factor
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side effects
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comorbidity
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tyrosine kinase
lung cancer
bevacizumab
breast cancer
diagnosis
marker
melanoma
dabrafenib
emt
interferon alpha
prostate cancer
vascular
bemcentinib
leukemia
bosutinib
epithelial
phenotype
cml
cell death
drug resistance
transcription factor
cytotoxic
immune treatment
prioritization
stathmin
imatinib
society
teaching

CCBIO Archive

Key elements in the history of CCBIO are well documented on our website (www.ccbio.no). Numerous reports and stories on scientific results, educational activities, communication cases and appearances in the media can be reviewed and reflected on. Here you will find some examples.

CCBIO Website →

CCBIO in a Nutshell →

The Hyperion Imaging System →

The Laser Microdissection System →

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2022

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New staff member in the CCBIO administration

Yamila Torres Cleuren joined CCBIO in 2020 as research advisor in a shared position with Neuro-SysMed. Yamila has a successful track-record of securing international research grants, and uses her experience in supporting CCBIO members in their application needs and strategic discussions. Y amila is Dutch/Spanish and she has had a very international career prior to joining CCBIO. She obtained her MS from King's College London in biomedical and molecular sciences research, and her PhD from a shared project between the University of Auckland, New Zealand and the University of California Santa Barbara, USA. She came to Bergen for her postdoctoral fellowship in 2016, developing new molecular biology and bioinformatics methods to study RNA biology.

List of Personnel at CCBIO 2020

Name	Position	Academic title	Group
Aae, Liv Rebecca Arnedatter	Senior executive officer	MA	Administration
Akslen, Lars A.	Professor, CCBIO director	MD, PhD	Akslen
Alam, Jahedul	Postdoc	PhD	Gullberg
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 researcher	MD, PhD	Akslen
Askeland, Cecilie	PhD candidate	MD	Akslen
Azeem, Waqas	Senior engineer	MS, PhD	Kalland
Aziz, Sura Muhammed	Senior researcher	MD	Akslen
Bakke, Ragnhild Maukon	Medical Student Research Program	Stud. Med.	Kalland
Benjaminsen, Susanne	Staff engineer	MS	McCormack
Bentsen, Pål Tore	PhD candidate	MD	Gjertsen
Berg, Hege Fredriksen	PhD candidate	MS	Krakstad
Berge, Sissel Vik	Chief engineer		Lorens
Beroukhim, Rameen	Adjunct researcher	MD, PhD	CCBIO
Bertolaso, Marta	Adjunct professor	PhD	CCBIO
Bjørge, Line	Adjunct professor	MD, PhD, MBA	Bjørge
Bjørnstad, Ole Vidhammer	PhD candidate	MS	Akslen
Bjånes, Tormod Karlsen	PhD candidate	MD	McCormack
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	Medical Student Research Program	Stud. Med.	Krakstad
Brekken, Rolf	Adjunct professor	MD, PhD	CCBIO
Bremer, Anne	Researcher	MA, PhD	Strand

Name	Position	Academic title	Group
Cairns, John	Adjunct professor	MA, MPhil	Health Economy
Campioni, Gloria	PhD candidate (guest student)		Costea
Castells, Oriol	Research assistant	MS	Gjertsen
Chen, Ying	PhD candidate	MD	Akslen
Cleuren, Yamila Torres	Senior advisor	PhD	Administration
Costea, Daniela Elena	Professor	DDS, PhD	Costea
Das, Ridhima	PhD candidate	DDS	Costea
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
Disha, Nazia Islam	Master student		Gullberg
D'Mello, Stacey	Postdoc	PhD	Lorens
Dongre, Harsh	Postdoc	NanoMS, PhD	Costea/Bjørge
Dowling, Tara Helen	PhD candidate	MS	Gjertsen/McCormack
Dybvik, Julie	PhD candidate	MD	Krakstad
Dyrkolbotn, Kjetil	Senior executive officer	MA	Administration
Edelmann, Reidunn Jetne	Accociate professor	MD, PhD	Akslen
Ehsani, Rezvan	Postdoc	PhD	Jonassen/Akslen
Eide, Agnes Jørgensen	Medical Student Research Program	Stud. Med.	Krakstad
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Eriksen, May Gjerstad	Staff engineer	MS	McCormack
Espedal, Heidi	Postdoc	MS, PhD	Krakstad
Fagerholt, Oda Helen Eck	Medical Student Research Program	Stud. Med.	Gjertsen
Fandalyuk, Zinayida	Staff engineer	MS	McCormack
Finne, Kenneth	Senior engineer	MS, PhD	Akslen
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Forsse, David	PhD candidate	MD	Krakstad
Forthun, Rakel Brendsdal	Researcher	MS, PhD	Gjertsen
Fosse, Vibeke	Researcher, veterinarian	DVM	McCormack/Bjørge
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Gabra, Hani	Adjunct professor	MD, PhD	CCBIO
Gabriel, Benjamin	Researcher	PhD	Kalland
Gabrielsen, Tommy Staahl	Professor	MA, PhD	Health Economy
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Gelebart, Pascal	Researcher	PhD	McCormack
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Gjerde, Christiane Helgestad	PhD candidate	MS	Bjørge/McCormack
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Smeland, Hilde Ytre-Hauge	PhD candidate	MS, PhD	Akslen/Gullberg/Reed
Solheim, Marion	Senior advisor		Administration
Stefansson, Ingunn	Professor	MD, PhD	Akslen
Stenmarck, Mille Sofie	Guest researcher	Cand.Med.	Strand
Stigen, Endre	Staff engineer		Lorens
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	Medical Student Research Program	Stud. Med.	Akslen/Wik
Sværi, Bård Kjetil Bratli	Leading research technician		Technical support
Syrtveit, Astrid	Medical Student Research Program	Stud. Med.	Wik
Sæle, Anna Kristine Myrmel	PhD candidate	MD	Akslen/Wik
Sødal, Marte	Master student		Krakstad
Sørlie, Therese	Adjunct professor	MD, PhD	CCBIO
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Tegnander, Amalie Fagerli	Medical Student Research Program	Stud. Med.	Akslen/Wik
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Thiery, Jean Paul	Adjunct professor	MD, PhD	CCBIO
Thodesen, Elisa Ulvøen	Staff engineer	MS	McCormack

Name	Position	Academic title	Group
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Torkildsen, Cecilie Fredvik	PhD candidate	MD	Bjørge
Tornaas, Stian	PhD candidate	MS	Costea
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	MS	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
Willoughby, Robert	Master student		McCormack
Wimalarasan, Akilina	Master student		Jonassen
Winge, Ingeborg	Senior engineer	PhD	Akslen
Xenaki, Victoria	PhD candidate	DDS	Costea
Zaraq, Tariq Jan	Master student		Costea
Östman, Arne	Adjunct professor	MD, PhD	CCBIO
Øyan, Anne Margrethe	Senior scientist	MS, PhD	Kalland
Åse, Hildegunn Siv	PhD candidate	MD	Krakstad

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