Centre for Cancer Biomarkers

Norwegian Centre of Excellence – University of Bergen

Norwegian Centre of Excellence

The Research Council of Norway

ANNUAL REPORT 2021

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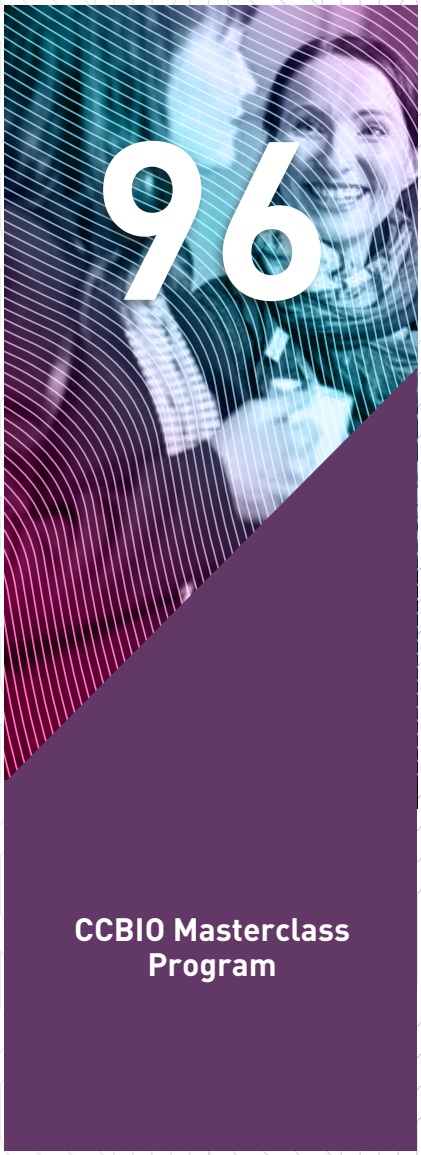

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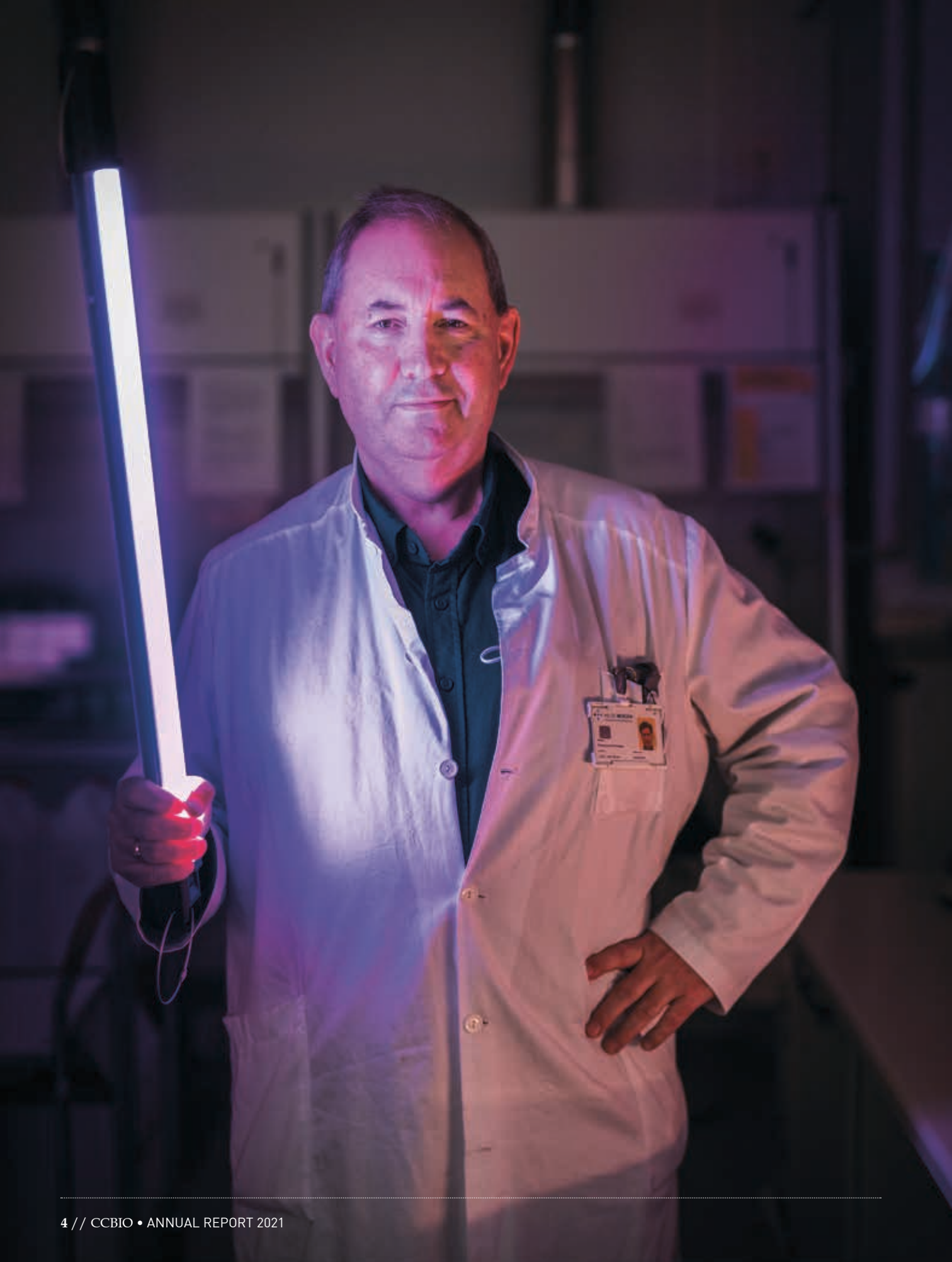


DIRECTOR'S COMMENTS

Through 2021, we have again experienced repeated transitions between hope and disappointment - in our lives and in the way science can be done. By continuous adaptations and professional plasticity, we have learned to keep working and do our best to achieve our short-term and long-term goals. Quite unexpected, the mysterious "omics of omicron" turned out to represent some optimism more than the opposite. By the end of the year, things were slowly getting back to normal - or the "new normal".

Our center has kept up its activity and pace as much as possible. The CCBIO Annual Symposium on May 19-20, 2021, was again organized - as a digital event this year, but with increased attendance and significant international presence and visibility. Several world-class scientists participated, such as Bernd Bodenmiller, Hans Clevers, Klaus Pantel and Morag Park. The many discussions were lively and fruitful. In particular, speed-presentations by in-house and external PhD candidates and postdocs were refreshing and most stimulating.

From the fall season, a couple of events should be mentioned. By "hybrid presentation", Robert S. Langer, Massachusetts Institute of Technology, presented the Falch Lecture (UiB) entitled "Creating and implementing breakthrough technologies in biotechnology and nanotechnology". Around 200 people enjoyed a truly inspirational talk from a "scientific giant". Remembering his early mentor, the late Judah Folkman, Langer motivated the audience to pursue ideas and keep asking fundamental questions. In 2021, Bjørn Tore Gjertsen, co-director of CCBIO, received the prestigious King Olav V's Prize for Cancer Research. In a celebration seminar organized by CCBIO, Gjertsen was praised for his tireless efforts as a translational scientist and as a devoted clinician.

We have realized the deep importance of personal proximity in science. Although hyper-communication by Zoom or other platforms might be quite efficient in some settings and for brief updates, the importance of on-site contact cannot be over-estimated. The science culture is dependent on mingling and small talk at meetings, and we therefore look forward to the upcoming 10th CCBIO Annual Symposium, to be arranged in-person on May 10-11, 2022.

CCBIO has continued to present significant findings in the biomarker field, ranging from development of new experimental models and methods, to the description of signaling pathways and spatial architecture at the single-cell level in malignant tumors. Notably, functional diagnostics represent a key development in real-time monitoring and fine-tuning as a basis for adaptive therapy and has been developed further. From our ELSA-team, an important thesis was defended this year, "Precision and Uncertainty" by Eirik J. Tranvåg. Finally, several significant grants and important recruitments have been landed.

Three CCBIO Opinion pieces are included in this report. Strell presents an update on possibilities and challenges of spatial mapping techniques. Reed gives an introduction to the important and difficult field of how to handle personal data in contemporary biomedical research and points to the necessity of international coordination. Bertolaso provides an intriguing analogy on how cancer research can be understood from a more philosophical point of view. Take your time and reflect on these comments.

At this point, we still have to modify and redefine some of our activities in science. We have experienced the perils of the pandemic, and nothing should be taken for granted – in science and in life. As we are turning another corner, we should more than ever stick to the core values of critical thinking, communication, and collaboration. ••

Lars A. Akslen, Director of CCBIO

VISION AND RESEARCH AREAS

CCBIO aims to discover, validate and translate cancer biomarkers to improve our understanding of tumor mechanisms, promote accurate diagnosis and stratification of cancer, and inform precise, cost-effective and responsible treatment of cancer.

CCBIO is especially focusing on the tumor microenvironment in primary and metastatic cancers, and how tissue context can define aggressive tumor traits and predict cancer behavior and prognosis. The center is studying how crosstalk between tumor cells and tumor microenvironment niches reflects functional cancer complexity and heterogeneity at various levels.

CCBIO concentrates on the following integrated and overlapping programs:

1. **Mechanisms of Tumor-Microenvironment Interactions (Basic Studies)**
2. **Discovery and Validation of Cancer Biomarkers (Biomarker Mapping)**
3. **Clinical Applications and Early Trials (Clinical Studies)**
4. **Ethics, Economics and Priorities (Societal Studies)**

Biomedical projects are combined with ethics and economics research, focusing on how to fund and prioritize expensive cancer diagnostics and 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 (CCBIO's host department), 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 collaborator with contributions towards CCBIO both in terms of staff, facilities, such as the Clinical Trials Unit, and advanced equipment.

Research management

In terms of science management, CCBIO is organized in four integrated research programs with associated teams (basic studies, biomarker 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 for the increasing collaboration within CCBIO. In 2021, most meetings were held online.

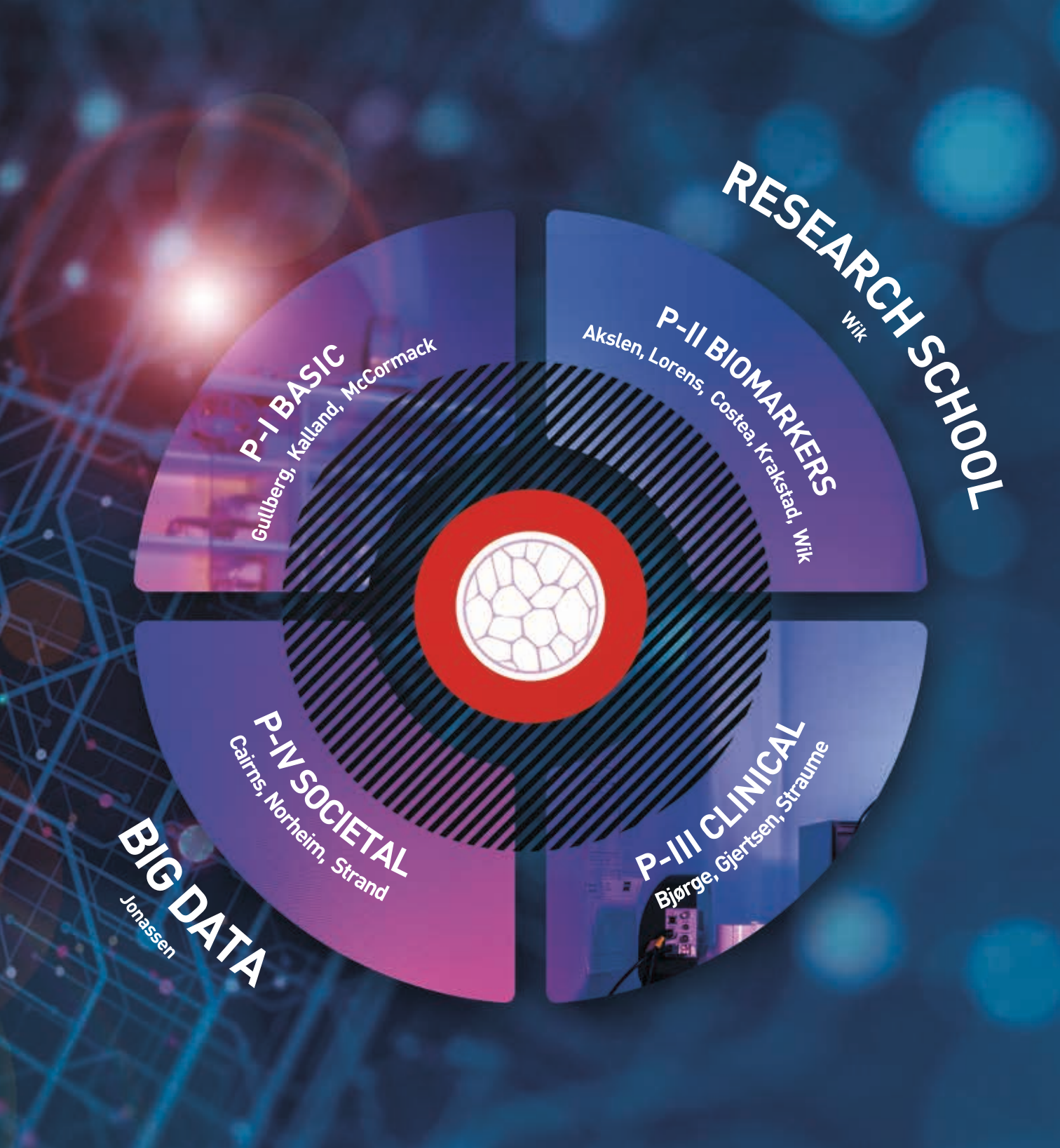
Management group

In 2021, 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 (Yamila Cleuren) and a strategic advisor (Rolf Reed) and assisted by the web- and newsletter editor (Eli S. Vidhammer), an economy coordinator (Mildrid B. Høgås), a PhD coordinator (Kjetil Harkestad), several 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
Imaging mass cytometry
Proteomics - Bioinformatics

CLINICAL STUDIES
Infrastructure and logistics
Clinical Trials Unit HUH
Multicenter studies

CCBIO Opinion
Text: Carina Strell, CCBIO International Faculty

THE ADVANCEMENT OF SPATIAL MAPPING TECHNIQUES – POSSIBILITIES AND CHALLENGES

The single cell
It was a technical and biological revolution, starting with the introduction of single cell sequencing techniques, that led to the description and characterization of novel cellular subtypes and cellular activation states. Consequently, researchers have gained a more detailed understanding of the cellular processes in health and disease. However, with the spatial information of the tissue context being lost during the enzymatic cell isolation processes, the relationship between cellular neighborhoods remains hidden, which still represents a key drawback of single cell sequencing methods.

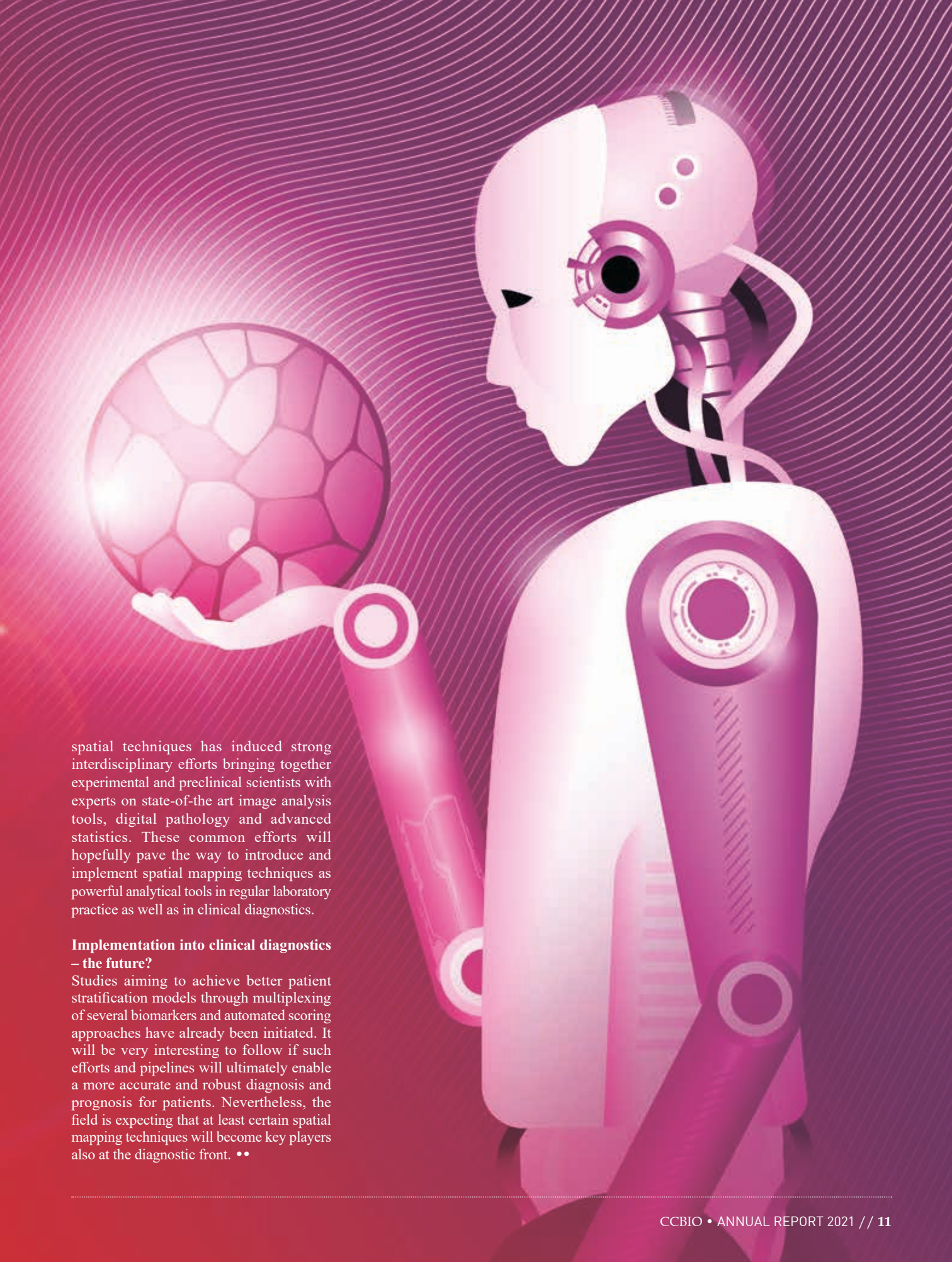
Traditionally, pathology approaches such as immunohistochemistry or RNA *in situ* hybridization, have been standard tools to detect the spatial distribution of a defined target of interest within the tissue context. However, in light of the increasing amount of novel single cell data, these traditional approaches, with their limited ability to upscale the target number, have become insufficient to visualize complex contextual phenotypes.

Location matters – cellular ecosystems
Pathologists, who work with the analysis of tissue sections on a daily basis, have always pointed out the importance of the spatial context. This information is more than just defining the anatomic location of a single cell. Spatial context is the indispensable information needed in order to fully understand cellular phenotypes, their plasticity, their interactions and, ultimately, their functionalities. This concept of cellular ecosystems, where genomic and microenvironmental interactions in concert determine the phenotype of a cell, had been postulated based on previous histological observations, but have received fresh and redefined attention with the new analytical possibilities opened by the accelerating development of highly multiplexed spatial mapping techniques.

Spatially mapping approaches currently cover a range from multiplexed protein detection (e.g. CODEX, Hyperion imaging mass cytometry) over RNA mapping (targeted: MERFISH *in situ* sequencing; untargeted: FISSEQ) to NGS based spatial transcriptomics (spatial transcriptomics); and some arising tools which combine both, RNA and protein detection. The high degree of multiplexing is achieved through different strategies including amongst others heavy-metal tagging of antibodies, or bar-code labeled probes, or iterative imaging cycles. Spatial mapping adds a deep informational layer to classical histology, revealing the expression of dozens of genes or proteins in one and the same tissue section, ideally at a single-cell level or even with subcellular resolution. These quantitative spatial insights allow us to gather new perspectives on disease progression or developmental processes. It is thus very understandable that researchers from almost any biological and medical field have been waiting for this technological advancement for years.

Challenges and possibilities ahead
Nevertheless, the overall excitement of the new spatial analysis tools is slightly shadowed by some technical challenges that still need to be overcome to make these approaches robust experimental tools for a laboratory day-to-day basis. Technical obstacles such as impaired sensitivity and/or specificity, low cellular resolution, and low sample throughput, often make spatial mapping approaches laborious to establish and use. Many of the spatial techniques are based on a fluorescent read-out and thus are easily impacted by tissue autofluorescence as well as staining artefacts. Consequently, each generated image and marker needs to be carefully reviewed and evaluated by pathologists. The implementation of spatial mapping approaches in the experimental design therefore requires careful considerations, weighting the *pros and cons* of one approach against the other. Shall one go for protein or RNA mapping, which sample type can be analyzed, how many markers are required, and which sensitivity and sample throughput is needed in order to obtain data that will answer the hypotheses or allow meaningful exploratory analyses. These decisions should always be reflected within the actual scope of the study. Finally, especially for young PIs, financial aspects come into the picture, as spatial experiments are still within the higher cost range.

Another, though highly exciting challenge, concerns data analysis and especially the interpretation of high-dimensional data. New computational algorithms are necessary to handle, relate and statistically analyze the compiled spatial data. Many analytical tools start with the problematic process of the accurate segmentation of single cells in the tissue context, which actually is the prerequisite to successfully interpret spatial phenotypes. Alternative approaches using pixel classification, AI or probabilistic cell phenotyping are increasingly considered and becoming established. In other words, the availability of new and highly multiplexed



spatial techniques has induced strong interdisciplinary efforts bringing together experimental and preclinical scientists with experts on state-of-the art image analysis tools, digital pathology and advanced statistics. These common efforts will hopefully pave the way to introduce and implement spatial mapping techniques as powerful analytical tools in regular laboratory practice as well as in clinical diagnostics.

Implementation into clinical diagnostics – the future?

Studies aiming to achieve better patient stratification models through multiplexing of several biomarkers and automated scoring approaches have already been initiated. It will be very interesting to follow if such efforts and pipelines will ultimately enable a more accurate and robust diagnosis and prognosis for patients. Nevertheless, the field is expecting that at least certain spatial mapping techniques will become key players also at the diagnostic front. ••

CCBIO Opinion
Text: Rolf Reed, CCBIO Strategic Advisor

SAFEGUARDING PERSONAL DATA: INTERNATIONAL COLLABORATION AND SHARING OF DATA ON HEALTH RESEARCH

The era of omics data and computing has opened and will still open new possibilities for analyzing health data to search for disease mechanisms and evaluate treatment. Biomedical and biological data need to be linked to information about the person from which it originates, in order to achieve its full potential for research and evaluation of treatment. The basis for using such data and biological material is an informed consent from the person who provides the data and agreement between the researcher and the person providing the data and material, with regard to what it will be used for, as well as how the data and information are safeguarded.

Medical research and researchers, and maybe more in the cancer field than in other disciplines, constitute an international collaborative endeavor where networks across national borders are fundamental. This raises issues on how data regarding the individual can be protected in accordance with rules and regulations as well as the agreement between the researcher and participant in the study. The law governing such an agreement is the law in the country where the agreement was made and signed. Care must be taken to protect personal data and the identity of the person signing into a clinical trial. Combining with other data, e.g. socioeconomic information, the risk of inadvertently being able to identify a person rises.

The differences on safeguarding personal data in different legislations within and between the EU and the US have had several implications. The basis in the EU is the GDPR (General Data Protection Regulation)[1] that went into effect in 2018. A fundamental challenge is the statutory conflicts between GDPR and the legislation of other countries. For example, US federal institutions are protected by sovereign immunity with the implication that non-US citizens cannot sue such institutions in case of illegal use of their data.[3]

The collaboration between national institutes of health and EEA countries is immense; in 2019 there were 5000 ongoing projects, of which 100 were of Norwegian origin. [4,5] While these projects are affected, some that do not require new data transfers have still been able to finish. What is perhaps more serious is the inability to find transfer mechanisms for new research projects.

The Schrems II judgement in the European court and new guidance from the European Data Protection Board have added both clarity and complexity to the challenges. The Norwegian research infrastructure for health data, "Helseanalyseplattformen",[6] that had intended to use an American cloud-based solution is currently put on pause as a consequence of the incompatibility between US and European legislations.

The implications for the long research ties between the EU and the US are disturbing and has resulted in a joint report and statement from three umbrella organizations of academies of sciences, European Academies of Science Advisory Council (EASAC), Federation of the European Academies of Medicine (FEAM) and All European Academies (ALLEA). [7]

During the last years, there is an increasing trend from journals that data should be published along with the paper itself. In this context, it is important to remember that the regulations governing such publications for researchers in the EEA area are those of the GDPR and not those of the country of the editorial office. [3]

Traditionally, genomic data have attracted most focus when it comes to be safeguarded and protected as personal data. Proteomics data have to a large degree been entered into open and accessible databases. However, with refined and improved tools for analyses, a discussion is emerging on how to safeguard personal data also when using this technology since "Plasma proteomes can be re-identifiable and potentially contain personally sensitive and incidental findings" as to whether also proteomics data need to be treated more in line with genetic data. [9]

Safeguarding personal data is important and the basis for trust between patients and researchers and need to be guarded carefully. The solution lies with the politicians to find agreements that balance personal data protection and advancement of science. Such advancement is a basis for health care and welfare of their citizens and occurs in a process which also involves international collaboration. ••

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CCBIO Opinion

Text: Marta Bertolaso, CCBIO International Faculty

EXPLAINING A SOCCER MATCH USING OMICS?

Imagine you are an extraterrestrial scientist observing soccer stadiums on Earth. These strange stadiums/cells present on the surface of the planet are sometimes full of fans/proteins and at other times empty. When they are full, you can detect a variety of noises that coincide with different things happening inside the nucleus of these stadiums/cells.

A new advanced technology allows you to identify and map what is inside the nucleus of these stadiums/cells: 22 players/chromosomes clearly classifiable into two different groups by mapping specific expressed "antigens" on their uniform/surface.

A deluge of data floods your computers. These players/chromosomes seem to be correlated by an unidentified law. Depending on the positions of these players/chromosomes in the nucleus, the fans/proteins positioned around the border of the stadiums/cells emit different noises. There is a cycle of 90 minutes of activity followed by a week of lethargy in these stadiums/cells.

These cells cause many problems in the correlated microenvironment: a few hours before the activity begins in them, many substances invade the space around them. The entire microenvironment presents the characteristic signs of stress and inflammation.

On your planet, this situation is called "cancer". Your department provides you with generous financial support for your research aimed at better understanding these strange pathologic processes and finding a remedy for them.

After several years of work, you have been able to identify white filaments at the core of the cell, a membrane composed by green villi on which the 22 players/chromosomes move, and a resistant shell that protects the stadiums/cells.

Finally, you discover the "magic ball": a white molecule that drives the entire system. Depending on the position of this "magic ball", the noise emitted by the stadiums/cell and the position of the 22 players/chromosomes change.

All your efforts are now focused on mapping every possible position of this "magic ball" and correlating these positions with those of the 22 players/chromosomes and the noise emitted by the cell.

The solution is now clear: destroy the "magic ball". Once it has been eliminated, the "cancer" will heal.

Can we learn something from this story as an analogy to the way we approach the study of cancer, its complexity and all the molecular data we are collecting? What was the extraterrestrial scientist doing wrong?

For us, who know the rules of a soccer match, it is easy to understand the "epistemological error" of our extraterrestrial scientist. The ball is not the cause of all the systems' dynamics, even if all the parameters seem to be correlated to it. It is quite an impossible task to grasp the rules of soccer just by mapping the ball's position during the time of the match. Are we making the same error in our cancer research?

I think this question should be better investigated in order to give a deeper biological meaning to all the data we are collecting from all the experiments performed in biomedical cancer research. ••

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Text: Roger Strand, CCBIO

TOWARDS A SENSIBLE IMPACT ASSESSMENT

In the language of the Aymara, an indigenous people of South America, the past is conceived as something in front of you while the future is behind you (Núñez & Sweetser, 2006). This makes a lot of sense. We have a picture of the past whereas the future is hidden to us. This is why impact assessments do not make sense until after or at the very end of a project.

2023 is the final year of the Centre of Excellence core grant awarded to CCBIO from the Research Council of Norway for the first 10 years of this enterprise. The centre will continue to exist and deliver cutting edge research, but possibly in a different organizational form. During 2022 and 2023, we will systematically describe and analyze our multiple activities and results with an eye for their real (present) impacts as well as their imagined (future) impacts. Rather than the usual perfunctory exercise of final reporting as required by funding bodies, such as a rather simplistic bibliometric assessment, our ambition is to create a knowledge synthesis that can dig deeper and answer our own questions: What have we done these 10 years? What did it lead to? What did we achieve of importance?

The impact language is not useless in this regard. Conventionally, it presents linear causal pathways:

Activity→Output→Outcome→Impact

In this scheme, outcomes are thought of as short- or middle-term consequences of results, while impacts are associated with the long term and the distal end of the chains. Since reality is notoriously non-linear, multi-dimensional and causally entangled, the methodological problem of causal attribution is in many ways worse in impact assessment than, say, in biological systems. With cells, there is at least the possibility to do another experiment.

Among our outputs, there are close to 1,000 research communications, dozens of PhD degrees, books, numerous dissemination and outreach events, clinical trials, new research infrastructures, and more. The outcomes include e.g. new findings and facts, models, methods, and explanations.

Notably, a new generation of cancer biomarker researchers is a key output from CCBIO, e.g. from the Masterclass program, and here lies a potential for lasting and expanding impact. Also, numerous strengthened or new collaborations with scientists, industry and policymakers is an essential outgrowth from the CCBIO environment. The impact is a question about causality but also one about importance: What did it lead to?

As noted in a previous annual report, in the era of social media and communication officers, extraordinary impact tends to get special appreciation – TV appearances, Lancet papers, et cetera. While this is certainly not unimportant as part of the contemporary political economy of science, our focus is also on normal impact: The steady creation of new findings, deeper understandings, and improved connections with clinical and societal institutions. Scientific and bibliographic impact rarely coincide.

Without rushing to conclusions, we expect that one profound impact of CCBIO is the creation of a new generation of scientists with a broad, interdisciplinary outlook that readily combine multivariate molecular information with clinical perspectives, and even economic, ethical, sociological and philosophical perspectives. In biomedicine, people normally last longer than scientific results. We are looking forward to an exciting challenge as we move into the phase of knowledge synthesis. ••

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SCIENTIFIC ADVISORY BOARD

The CCBIO Scientific Advisory Board (SAB) consists of Professors Carl-Henrik Heldin (chair), 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. Since physical presence is strongly desirable for such meetings, the SAB was not able to convene in 2020 and 2021 but will most likely meet again in the spring of 2022.

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 its groups to 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.

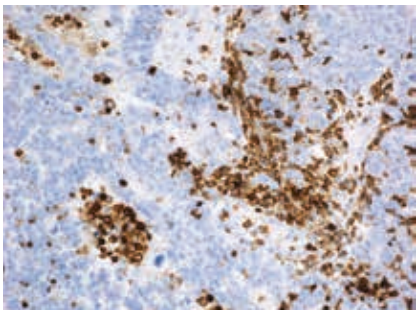
Ate van der Zee is professor of gynecological oncology and chairman of the Board of Directors at the University Medical Center Groningen, the Netherlands.

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 2021

CCBIO has a two-armed pipeline of biomedical (Team 1-3) and societal (Team 4) projects. The center has a focus on cancer biology and biomarkers related to tumor-microenvironment interactions in primary and metastatic lesions, including the expanding area of tumor immunology. The center concentrates on how biomarkers can define aggressive tumor phenotypes and predict tumor progression and therapy response. Societal studies of ethics, economics, priorities and philosophy represent an integrated aspect of biomarker projects within CCBIO and enhance self-reflection among researchers. All activities are performed in the context of interactive education and communication efforts.

During 2021, the COVID-19 pandemic was still a challenge in cycles of hope and disappointments. Laboratories have been up and running, although with reduced capacity and some delays. Courses and meetings were mostly 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 this experience, not only related to the disease itself and how it is handled, but also on how COVID has



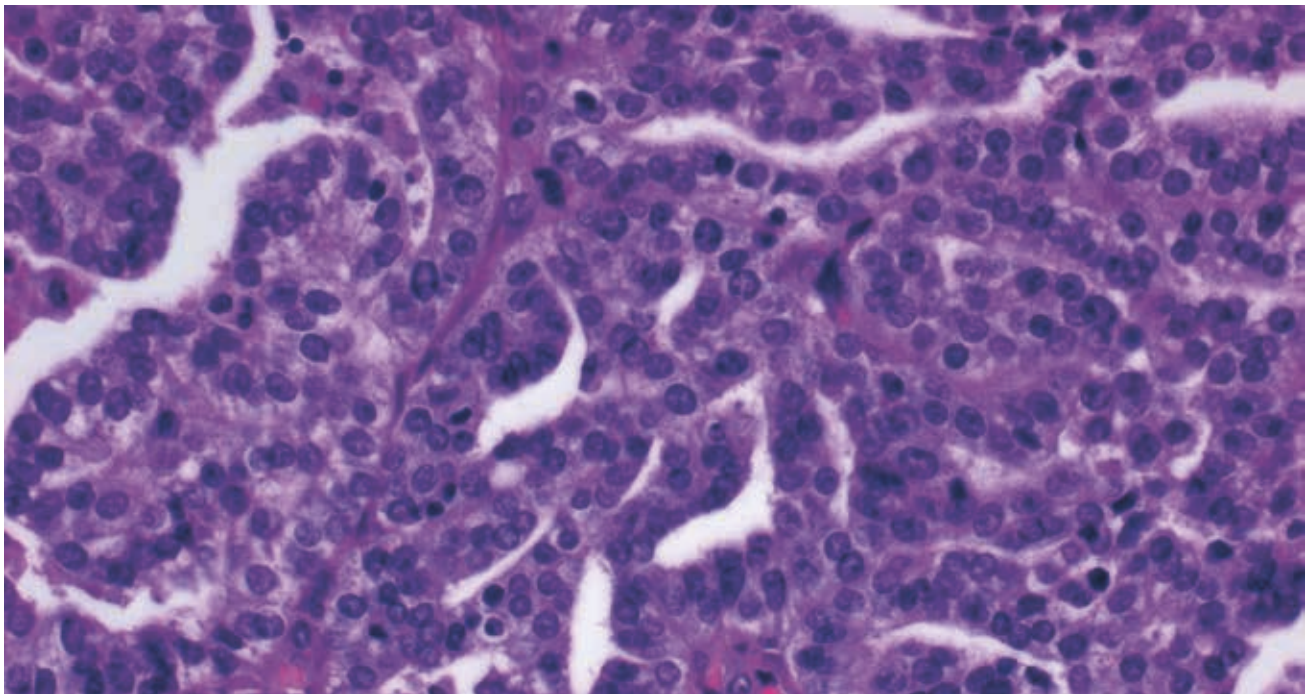
made us rethink and reinvent the ways we are communicating and working. As of today, the society has been reopened, and routines are slowly getting back to normal. Some new ways of doing things have come to stay.

The CCBIO Research School for Cancer Studies has continued to increase its activities. We now have 12 credit giving courses and a wide range of other activities. A strategic collaboration has been developed with the research school at Neuro-SysMed, an RCN funded Centre for Clinical Treatment Research (FKB) at the University of Bergen and Haukeland University Hospital. We believe that this will benefit both centers. The CCBIO Masterclass Program for career development has been an important activity for 8 selected candidates, and the second INTPART grant from the RCN is important for our international networking and the relationship with our partner - the Vascular Biology Program at Boston Children's Hospital and Harvard Medical School. The very successful two-day Scientific Writing Seminar was repeated in 2021 with 85 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, neurogenesis, 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 importance of integrin α11 in the tumor microenvironment, by the characterization of novel integrin α11 function blocking antibodies and development of a mouse model to explore the role of α11 in tumor stroma. Thus, in 2020-21, the group reported the development of a new fibroblast specific transgenic mouse strain (ITGA11-Cre driver mouse strain) where Cre-recombinase is driven by the integrin α11 promoter (Alam et al., Matrix Biol Plus 2020). Further development will enable direct visualization of the dynamic α11 expression in tissues and tumor stroma without fixation or other treatments. Second, the group continues epitope mapping of the novel function blocking α11 Ab 203E1. (Erusappan et al., Sci Rep 2020). A third project relates to the role of integrin α11 absence in the stroma of squamous cell carcinoma (SCC) and is performed in collaboration with Dr. Ritva Heljasvaara (University of Oulu).

In the **Kalland group**, focus has been on two strategies: drug discovery by repurposing, and the concept of cryoimmuno-based dendritic cell (DC) therapy. During 2021, a phase I clinical trial for cryoimmuno-therapy (CryoIT)



for patients with advanced prostate cancer was completed (Thomsen et al., in revision). Conceptually, immature DCs are placed in the inflammatory cryoablated prostate cancer tissue so that they may detect and process the entire panel of tumor-associated neo-antigens, accounting for tumor heterogeneity. Treatment effects were suggested according to radiology, circulating tumor cells, serum auto-antibody profiling, and ultradeep T-cell receptor sequencing. The group additionally works on biomarkers in order to obtain more precise results from clinical trials, including an *in vivo*-mimicking *ex vivo*-model of standardized tissue explants. A second CryoIT clinical trial is being prepared for start-up. 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 are studied (Azeem et al., Biomedicines 2021).

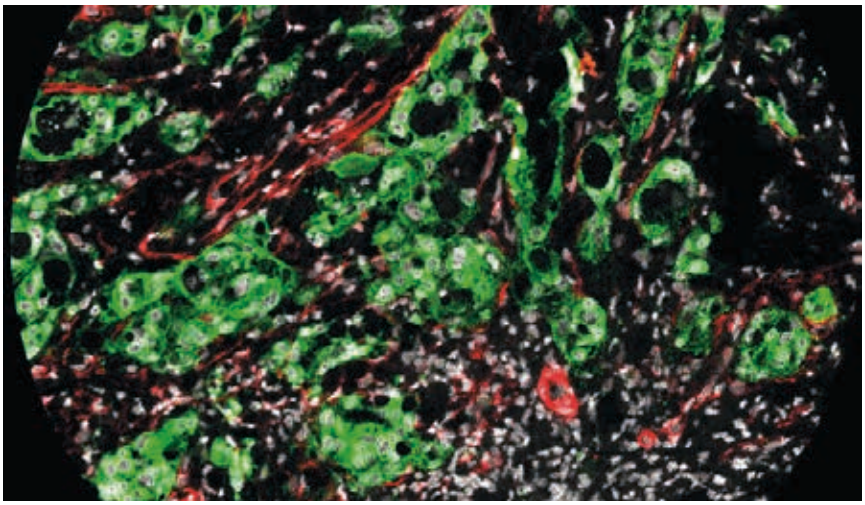
The **McCormack group** has had a major focus on the importance of studying appropriate preclinical models (organoids, PDX) before clinical trials are performed. Such models might improve therapy development, such as immunotherapy, and have been established and explored for gynecologic cancers, pancreatic cancers, and leukemias. Several imaging techniques have been studied, for example against CD24 (stem cell marker) in high-grade ovarian cancers from PDX-models with improved sensitivity in tumor detection and more precise cytoreduction surgery (Kleinmanns, Bischof et al., EBioMedicine 2020). Results demonstrate a 50% increase in the number of tumors detected and greatly improved extent of debulking (Kleinmanns, Fosse et al., EBioMedicine 2020). Strategies for improved drug delivery have been examined, for example by using sonoporation in the treatment of pancreatic cancer, showing how this might impact intracellular signaling of cancer cells with identification of biomarkers.

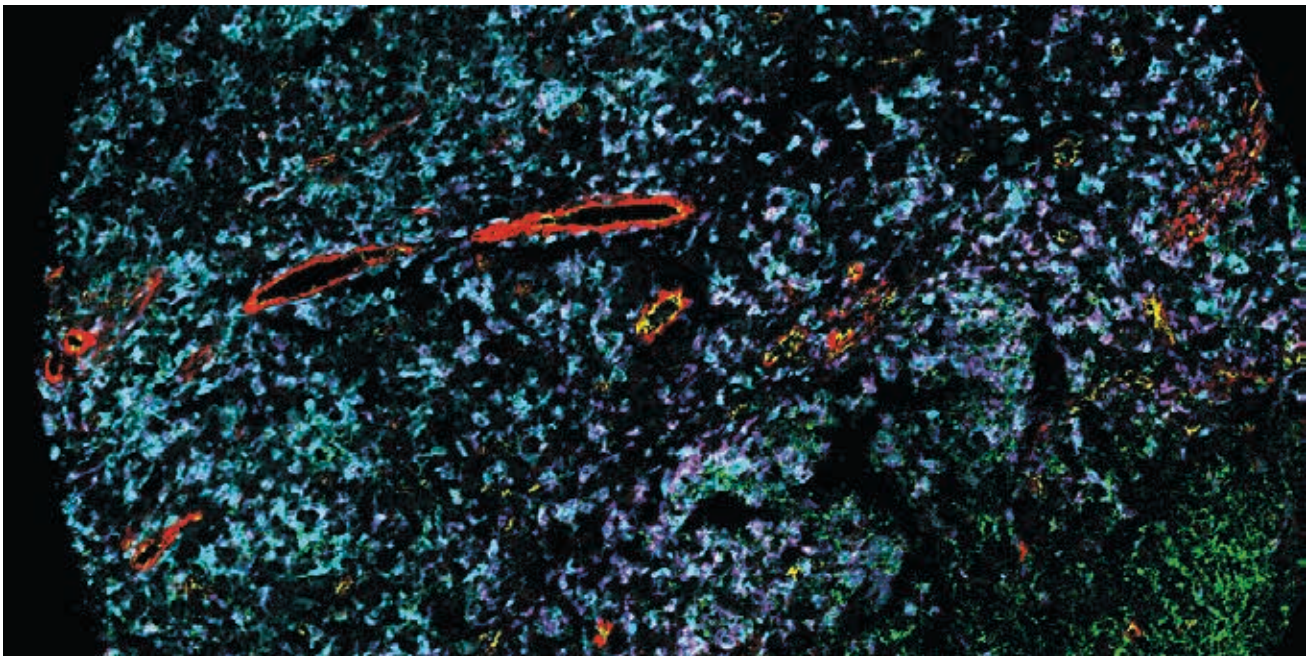
In **TEAM 2**, studies are being performed on biomarker discovery and validation in several tumors, with additional work on how markers are related to mechanisms

for tumor progress, such as immune responses, and the development of treatment. Candidate biomarkers are used to map tumor diversity including associations with clinico-pathologic phenotypes and patient outcome.

The **Akslen group** is currently working on spatial mapping of tissue biomarkers related to the tumor microenvironment in human breast cancer, for improved understanding of the underlying biology and more precise prognostication and treatment response prediction. The main focus is currently on profiling of luminal-like and basal-like breast tumors, by proteomics studies and imaging mass cytometry (IMC). These questions are asked: 1. Can the stromal breast cancer proteome (Mass Spectrometry) improve tumor stratification? (Finne et al., in submission). 2. How does the tumor proteome react to hypoxia in breast cancer subtypes? (Kjølle et al., in revision). 3. Does neurogenesis in breast cancer differ between molecular subtypes, and how does this trait relate to tumor progress? (Wik et al., submitted). 4. What are the roles of Nestin and Stathmin in aggressive breast cancer? Imaging mass cytometry (IMC) is used to map cancer tissue landscapes for high-order co-expression patterns and delineation of informative tumor niches (Askeland et al., in preparation; Ardawatia et al., in preparation). During 2020-21, 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 value of baseline microvessel density in predicting response to neoadjuvant bevacizumab treatment of locally advanced breast cancer was reported (Krüger et al., Sci Rep 2021).

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 relevant for resistance to immunotherapy. 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 2020-21, the team reported that AXL is a driver of stemness in normal mammary gland and breast cancer (Engelsen et al., iScience 2020), and they showed that AXL is a key factor in acquired resistance to EGFR targeted treatment in lung cancer (Lotsberg et al.,





J Thor Oncol 2020). Further, the group and collaborators reported that AXL is an important factor for cell plasticity and metastasis in pancreatic cancer (Du et al., Mol Cancer Res 2021). Results on the link between AXL and PD-L1 in renal cell cancer were also presented (Terry et al., Clin Cancer Res 2021).

The **Costea group** studies mechanisms of tumor-stroma interactions in oral and vulvar squamous carcinoma, with focus on metabolic changes in carcinoma associated fibroblasts (CAFs), and the association with genetic alterations including HPV subtypes and their role for tumor progression. The group studies the tumor stroma in drug resistance and as a source of prognostic biomarkers. During 2020-21, they presented how metabolic reprogramming of normal oral fibroblasts correlated with increased glycolytic metabolism of oral squamous cell carcinoma, by unidirectional mitochondrial transfer, reporting a "cancer-associated fibroblast metabolic phenotype" (Zhang et al., Cell Mol Life Sci 2020). The group published data on the role of microRNAs in tumor-stroma interactions and identified twelve differentially expressed miRs in stromal fibroblasts of OSCC lesions compared with normal oral mucosa (Rajthala et al., Int J Mol Sci 2021). A link between miR-204 and integrin α11 was found, and in a cohort of 169 patients with HPV-negative primary oral squamous carcinoma, the group showed that stromal presence of miR-204 predicted better overall survival and recurrence free survival (Rajthala et al., Cancers 2021).

In studies of gynecologic cancers by the **Krakstad group**, tissue and serum-based biomarkers as well as genetic landscapes 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 2020-21, the group reported on the development of prediction models for lymph node metastasis in endometrial carcinoma (Berg et al., Br J Cancer 2020), and also on maintained survival outcome after reducing lymphadenectomy rates and optimizing adjuvant treatment in this disease (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). A radiogenomics application for prognostic profiling of endometrial cancer was presented (Høivik et al., Comm Biol 2021). Also, genomic alterations in cervical cancers were reported (Halle et al., NPJ Genom Med 2021). Establishment of patient-derived organoids of endometrial cancers were published (Berg et al., Comm Med 2021).

The **Wik group** has a focus on breast cancer of the young and why these patients often experience a more aggressive disease behavior. A patient cohort has been established with multiple molecular and clinico-pathologic annotations, including primary tumors and metastases, and further genetic and imaging mass cytometric (IMC) 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. An age-related gene expression signature tightly linked to proliferation and prognosis has been identified (Ingebriktsen et al., in revision). Wik is directing the CCBIO Research School for Cancer Studies and is the local coordinator of the CCBIO-INTPART II collaboration with the Vascular Biology Program at Boston Children's Hospital and Harvard Medical School. During 2020-21, 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 established.

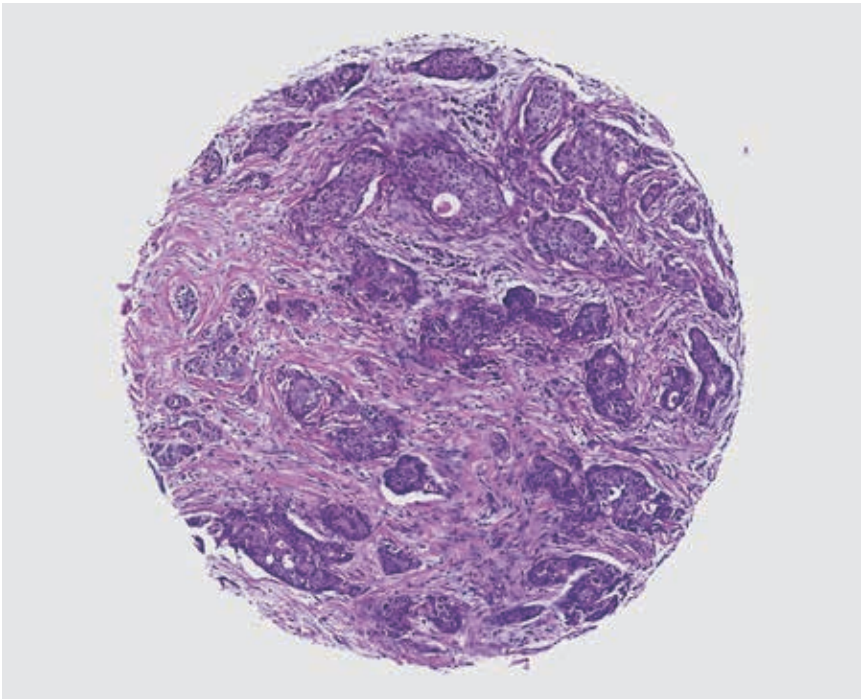
In **TEAM 3**, the main focus is to perform clinical trials with associated biomarker studies, and to promote novel findings on markers and treatments for clinical implementation and change of practice.

The **Gjertsen group** has been working on single cell biomarker profiling of leukemia and immune cells in solid tumors 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 signaling analysis can be used to monitor early responses in AML. In a new project, the CSF1R 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 clinical importance of p53 isoforms. During 2020-21, 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). Results on single cell detection of the p53 protein by mass cytometry were reported (Fagerholt et al., Cancers 2020). The group reported on differences in leukemic cells from males and females and the role of this confounding factor for risk stratification and guidance of targeted therapy (Hellesøy et al., Mol Oncol 2021). A position paper on liquid biopsies in solid cancers in a Nordic healthcare system was presented (Nordgård et al., Cancers 2021).

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. In 2021, data on ipilimumab treatment in metastatic melanoma from a phase IV trial was presented (Aamdal et al., Int J Cancer 2021).

The **Bjørge group** is engaged in novel multicenter trials with translational research programs related to high-grade ovarian cancer, aiming to improve patient stratification and treatment efficacy. 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 2020-21, 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 2021, the group reported on phenotypic profiling of the tumor microenvironment in ovarian cancer by using mass cytometry (Anandan et al., Cancers 2021).

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



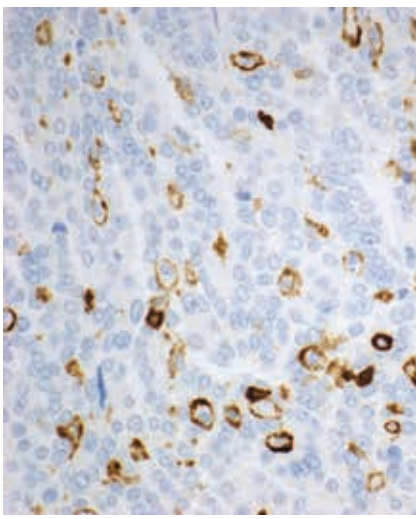
and therapies and in medical innovation. The main measure of this impact is ultimately its effect on the quality and cost-effectiveness of cancer management, whereas it cannot be precisely measured on the short-term. Better knowledge of cancer biomarkers is likely to affect the prioritization dilemmas, 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 and the coproduction of science, technology, and society.

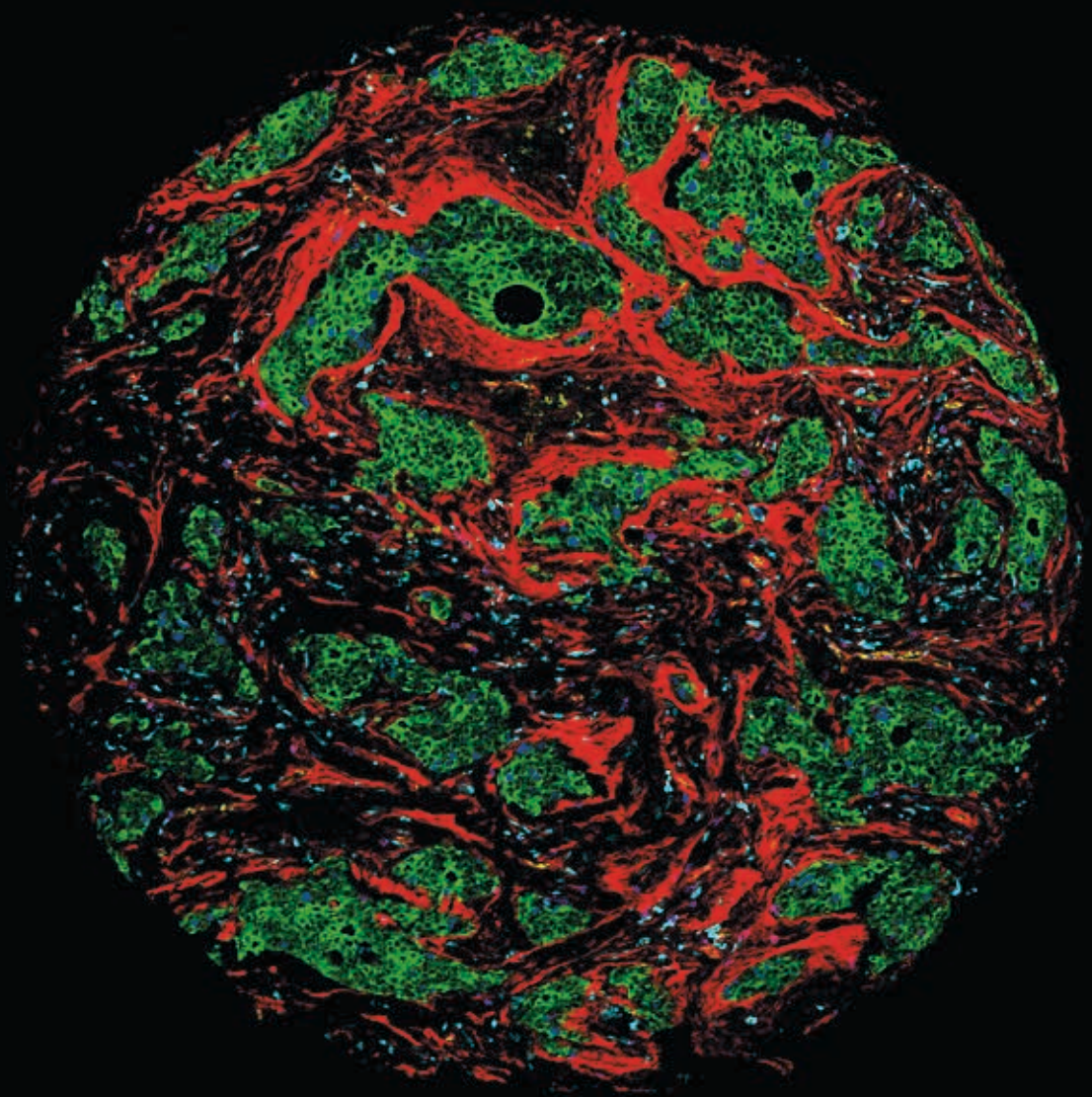
The **Strand group** performs research on the ethical, legal, and societal aspects (ELSA) of CCBIO's research, distinguishing between two interrelated goals; 1: A better understanding of the developments, expectations and imaginaries of personalized and precision cancer medicine, including its political 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). 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. In 2021, the group reached an important milestone: the submission of the interdisciplinary research anthology "*Precision Oncology and Cancer Biomarkers: Issues at Stake and Matters of Concern*", edited by Anne Bremer and Roger Strand (Springer 2022, in press). Also, during 2021, the key focus was interdisciplinary analysis of the sociotechnical imaginaries of personalized and precision cancer medicine, resulting in the above mentioned 16-chapter research anthology. In general, the group has searched for *re-framings* of cancer, which has been presented in the anthology, drawing on complexity theory, medical philosophy, Daoist philosophy, science and technology studies, post-normal science, health technology assessment et cetera. Strand believes this project can be seen as, if not finalized, at least reaching its final stage.

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 economists (**Cairns group**) and ethicists (**Norheim group**). 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



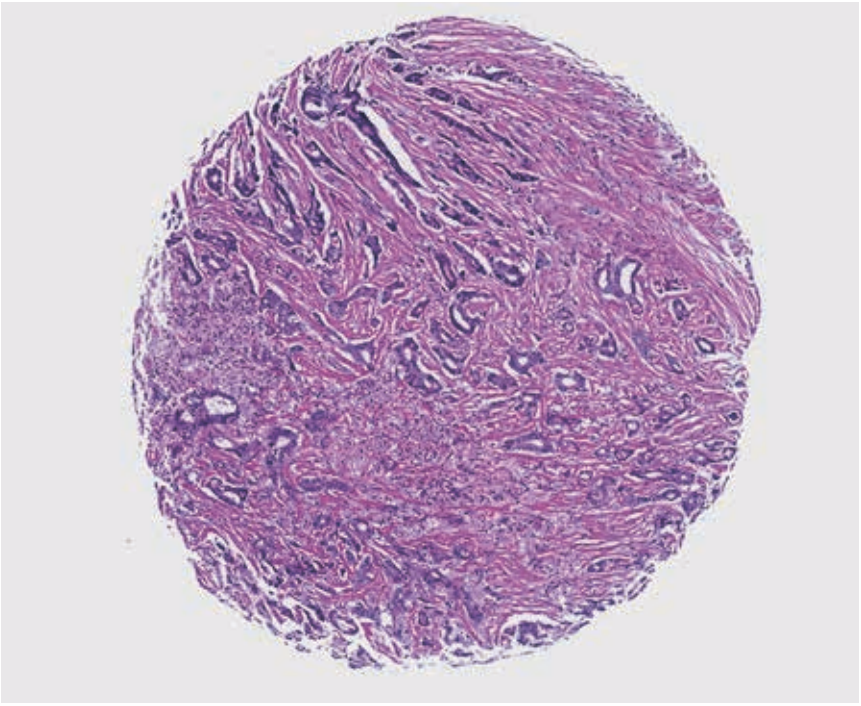
assessing the impact of cancer biomarkers on health outcomes in Norway (accepted for publication), and their results suggest that biomarker tests improve health by ensuring that the right treatment is given to the right patient and that the effect is stronger for cancer types for which fewer drugs are 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 D'Avó Luís titled "Essays on Economic Incentives and Implications of Biomarker Tests" was successfully defended at UIB in 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 the London School of Hygiene & Tropical Medicine) 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. During 2021, papers on development of biomarkers and health outcome (D'Avó Luis AB et al., Eur J Health Econ 2021), evaluation of cost-effectiveness of companion biomarkers (Seo et al., BMC Cancer 2021), and modeling of cost-effectiveness analysis (Seo et al., PharmacoEconomics 2021) have been presented.

In the **Norheim group**, an aim has been to map how cancer biomarkers can inform and hopefully improve health care priority settings, 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 2019-2021, 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 2021, Tranvåg successfully defended his PhD thesis "Precision and Uncertainty".

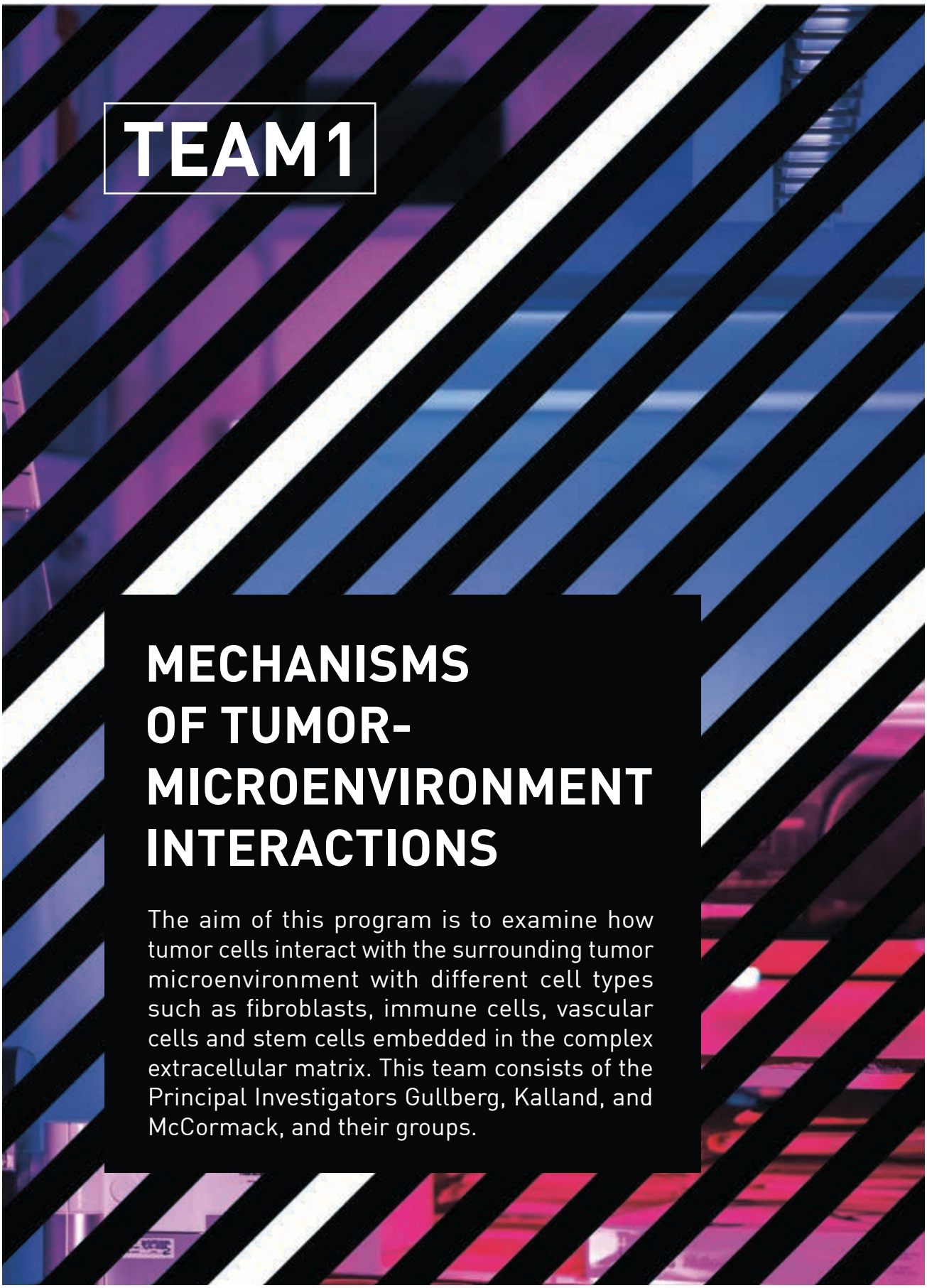
In addition to the activities in these teams, the **Jonassen group** has been actively collaborating across different groups on the systems biology features of many projects and processing of big data. During 2020-21, several such projects have been ongoing, like the ERAPerMed project "AML_PM – Improved treatment of Acute Myeloid Leukemia" (with Gjertsen). Postdoc Dimitrios Kleftogiannis, linked to this project, is also using parts of his time to work on breast cancer profiling with the Akslen and Wik groups. 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, and 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 and conducted during 2021, with 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 have four teams and corresponding project areas: basic studies of tumor-microenvironment interactions (Team 1), discovery 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, philosophy, 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 has taken place over the years. The center is supported by an International Faculty of 15 top scientists in different fields.



TEAM1

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.

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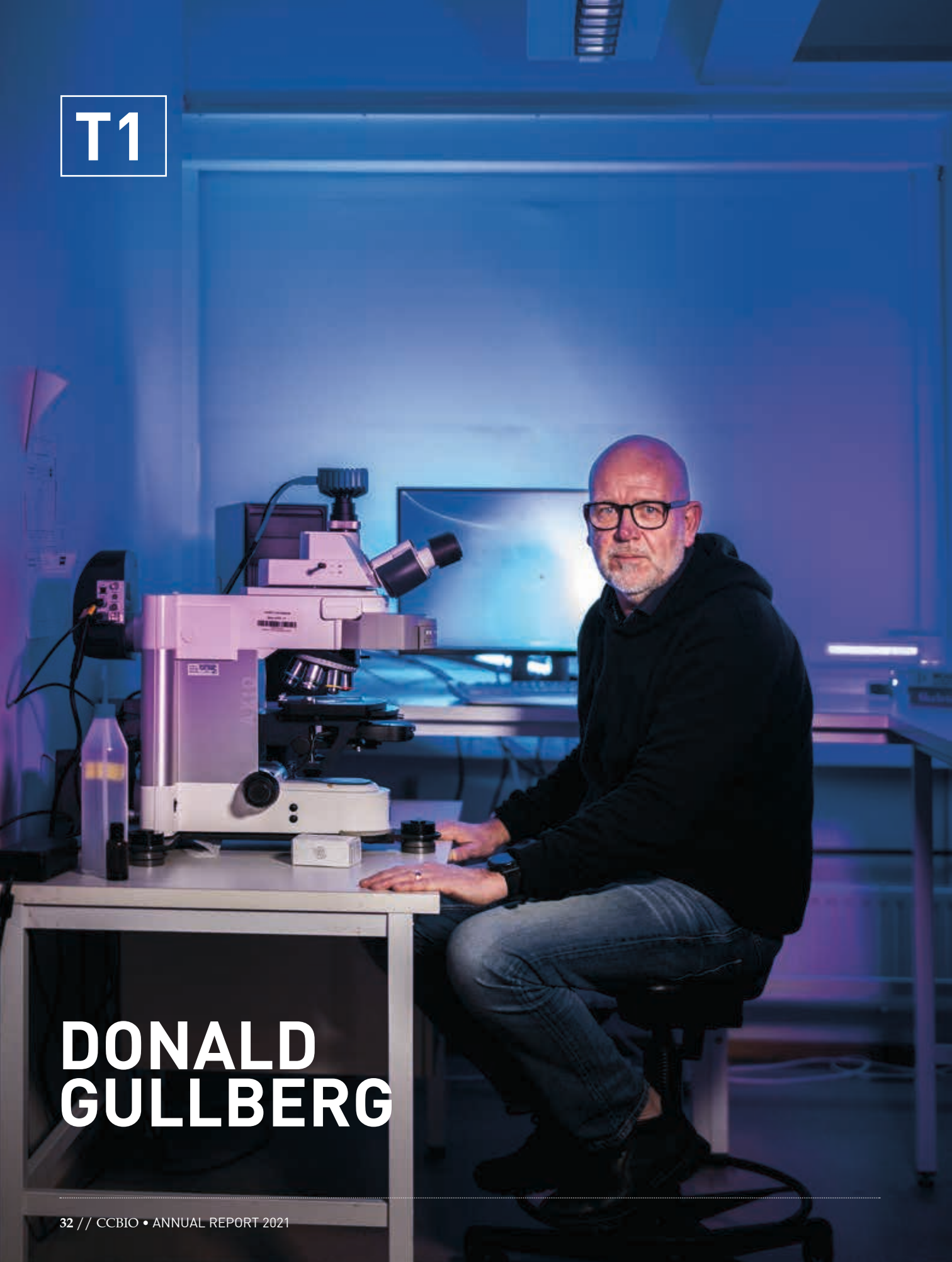


DONALD GULLBERG

Research focus
The research of the Gullberg group is focused on work related to integrin α11. 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 the 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., Matrix Biol. Plus, 2020). The Cre mouse strain is now being bred with a tdTomato strain for direct visualization.

2. A second CCBIO-supported project relates to the role of integrin α11 in skin 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 the mouse strain deficient in integrin α11. Due to the COVID situation, this project has been dormant, but as of January 2021, it has been activated by a collaboration with Daniela Costea (CCBIO, UiB) and Vel-Matti Kähäri, University of Turku. The idea is to complement the animal data with imaging mass cytometry data (Hyperion) from SCC material obtained from Finland.

3. A third project relates to epitope mapping of integrin α11 mAbs. The group has finished epitope mapping of mAb210F4 but is continuing with the function blocking antibody mAb203E1. This project is now reinforced by a PhD student financed by the Medical Faculty and a Norwegian Cancer Society supported postdoc who will start in 2022.

Important results
The finalization of the ITGA11-Cre mouse strain was a major milestone after 10 years of systematic work on this project. The detailed epitope mapping of mAb210F4 down to five amino acids also reflected persistent work on this project over a number of years.

Current challenges
Major challenges include finding funding for the projects, finding good candidates for MS, PhD and postdoc positions, and the restricted traveling situation, hampering active collaborations that would have benefitted from interactions of laboratory personnel.

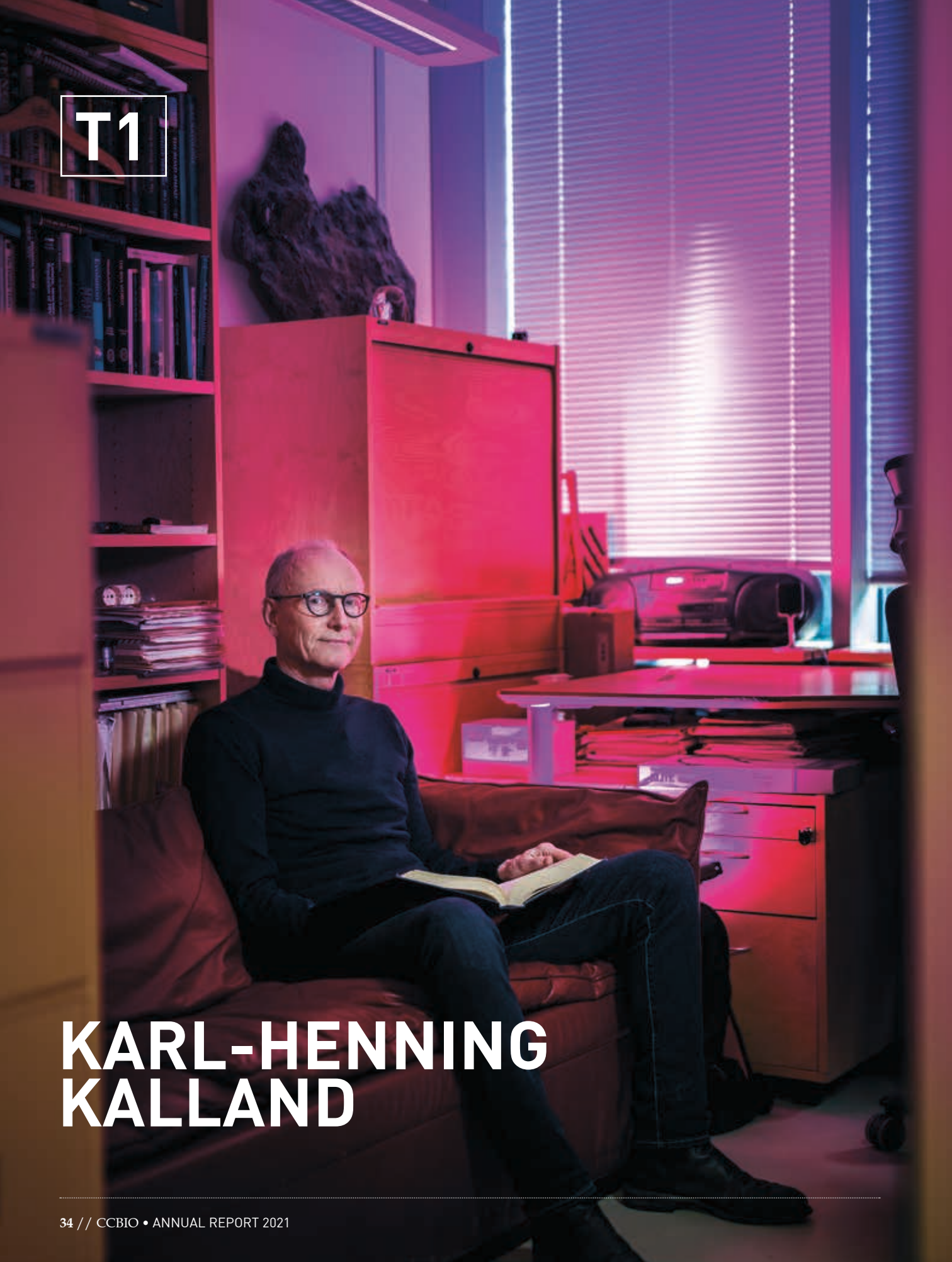
Focus and plans for the next two years
The overall goal is to continue characterization of integrin α11 to be able to evaluate its potential as a therapeutic target in fibrotic conditions, specifically:

1. Together with Ritva Heljasvaara, the group is crossing the ITGA11-Cre mouse strain with the double-fluorescent ROSA$^{mT/mG}$ 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. For the function blocking α11 mAb203E1 antibody, the group continues epitope mapping. They have sequenced the antibody and would now like to humanize the antibody, which is a costly project, but resources will be applied for. ••

GROUP MEMBERS:

Gullberg, Donald, PhD, professor, group leader
Kusche-Gullberg, Marion, PhD, professor
Disha, Nazia Islam, master student
Goni, Osman, master student
Grigorian, Andre, master student
Grønning, Mona, chief engineer
Lu, Ning, PhD, senior engineer
Mato, Raúl Pérez, MS, PhD candidate
Musiime, Moses, PhD, postdoc



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KARL-HENNING KALLAND

Research focus
The Kalland group is focusing on dendritic cell-based cryoimmunotherapy (CryoIT) as a new cancer treatment modality, with integrated drug discovery and development, as their main priorities.

Subprojects
CryoIT: Having completed a phase I clinical trial against metastatic prostate cancer, the group now prepares for the next phase clinical trial. The main efforts in 2021 and beyond are directed towards robust production of potent therapeutic dendritic cells (DCs) in Bergen.

Drug Discovery and Development: The screening part of this project has utilized both a panel of phytochemicals available in collaboration with Shanghai and a panel of drugs approved for treatment of human and animal diseases according to the repurposing strategy. Currently, the transcription factors STAT3, androgen receptor (AR), β-catenin and inhibitors of the enzyme Indoleamine 2,3-dioxygenase 1 (IDO1) are investigated.

Important results
CryoIT: Good manufacturing practice (GMP)-grade DCs and standard operating procedures are currently established using the Miltenyi CliniMACS Prodigy closed system. The DC product is compared to manually produced monocyte-derived DCs and conventional type 1 (DC1) and type 2 (DC2) which circulate in normal blood. Results that may be very important include the observations that when immature DCs mature *in vitro* according to widely used routine conditions, pro-inflammatory and tolerogenic features co-develop. Additionally, *in vitro* viability of DCs is compromised due to spontaneous apoptosis induction. Molecular and cellular control of such features could generate more potent therapeutic immune cells.

The European Patent Office has approved the patent application of CryoIT combined with intra-tumoral injection of an immune checkpoint inhibitor. The national implementation phase is ongoing. A manuscript reporting the results of the completed phase I clinical trial is still in revision rounds for publication.

Drug Discovery and Development: The group's repurposing strategy has previously published two compounds that inhibit β-catenin signaling in cancer cell lines. The molecular targets and mechanisms were identified. Novel compounds with STAT3-inhibiting activity have been discovered. One of the compounds exhibited dual inhibition of both androgen receptor (AR) and STAT3. Patent applications have been submitted and licensing is being negotiated with Xennials Therapeutics, Chicago, IL, USA, by Vestlandets Innovasjonselskap (VIS).

Current challenges
The main challenges will be:
1. Establishing Good Manufacturing Practice (GMP) grade production of therapeutic dendritic cells in Bergen for the CryoIT next phase clinical trial.

2. Revision of the CryoIT protocol with planning and funding of the next phase clinical trial.

3. Establishing a new *in vivo*-mimicking *ex vivo*-model of patient materials for new quality control tests of therapeutic cells and drug combinations.

Focus and plans for the next two years
The overarching focus and aim will be to develop enhanced immunotherapy against cancer. Kalland envisages a next stage clinical BASKET trial during 2022-2024 and a next generation CryoIT protocol in 2024/25. The BASKET trial will include patients with prostate cancer, kidney cancer and the gynecological vulvar cancer. The next generation CryoIT protocol will be enhanced by more robust and potent therapeutic dendritic cells. Biomarker development and implementation in the next clinical trial includes T-cell receptor sequencing and the *in vivo*-mimicking *ex vivo* culture model to assess lymphocyte and dendritic cell functionalities. ••

GROUP MEMBERS:

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

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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 RCN, NIH and Helse Vest explores the application of sonoporation in the treatment of pancreatic ductal adenocarcinoma (PDAC). PreLIM funded by the Norwegian Cancer Society and Horizon 2020 (AML VACCiN) focuses on the development of novel preclinical models of leukemias and lymphomas in the development of novel targeted and immune therapies as well as exploration of microenvironmental factors critical to disease development and emergence of resistant clones. Finally, funded through Helse Vest and a Marie Skłodowska-Curie Innovative training network (ISPIC) INOvA (Innovative Novel Ovarian cancer treatment Approaches), the group is developing the use of image-guided surgery, whereby fluorescent dyes will target biomarkers on surgically amenable cancers, to aid complete resection. They are planning studies in dogs in addition to 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 an 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 therapeutics intervention in combination with sonoporation (Haugse et al., Pharmaceutics 2020). Ragnhild Haugse and Tormod Karlsen Bjånes defended their theses 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 therapeutic target for mantle cell lymphoma (MCL) (Lazarian 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 collaborates with Dr. Davila at the Moffitt Cancer Center on development of new cell-based immunotherapeutics towards hematological malignancies and solid cancers (lymphoma-leukemia, ovarian cancer).

The INOvA team identified the tumor biomarker CD24 for 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 we develop and perform preclinical research.

Focus and plans for the next two years
The group will work to consolidate 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 will impact clinical development of tomorrow's therapeutics. ••

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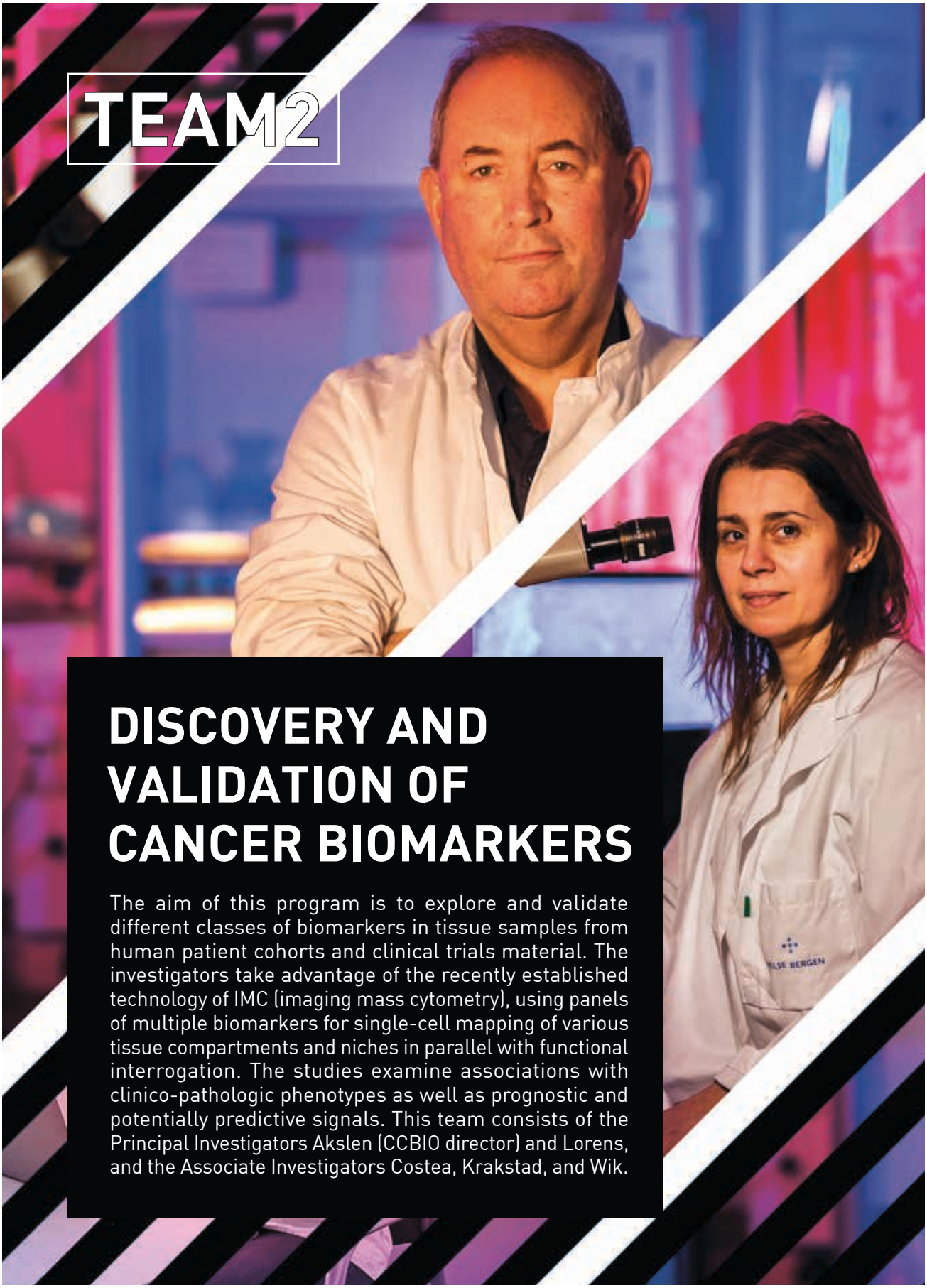

TEAM2

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 single-cell mapping of various tissue compartments and niches in parallel with functional interrogation. The studies examine associations with clinico-pathologic phenotypes as well as prognostic and potentially predictive signals. This team consists of the Principal Investigators Akslen (CCBIO director) and Lorens, and the Associate Investigators Costea, Krakstad, and Wik.

T2

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 biological understanding and better prediction of aggressive tumor behavior and treatment response. As part of precision pathology, such markers are expected to improve molecular classification and stratification of malignant tumors, and to aid precise management of the patients. The group concentrates on breast cancer proteomics (by Mass Spectrometry) and multi-marker spatial mapping of tumor landscapes (by Imaging Mass Cytometry).

Subprojects
1. Stromal proteomic patterns and stratification of breast cancer.

2. Breast cancer hypoxia responses at the proteome level.

3. Markers of cancer-neural interactions in primary and metastatic breast cancer.

4. Role of Nestin and Stathmin in BRCA1-related and basal-like breast cancer.

Important results
Proteomic profiling of laser capture micro-dissected breast cancer tissues has been performed by the group, separating cancer cells and microenvironment compartments. Stromal protein signatures are different between hormone receptor positive (luminal-like) and hormone receptor negative (basal-like) tumors, being prognostically independent of intrinsic molecular classification, also after external validation. For the first time, we demonstrate that a stromal proteome signature is able to split the luminal A breast cancers in low-grade and high-grade categories (Finne et al., submitted). Further, stromal protein profiles have been integrated with breast cancer cell line secretome data from baseline and after hypoxic conditions, demonstrating metabolic reprogramming, especially among luminal-like tumors, indicating subtype-specific metabolic responses (Kjølle et al., in revision).

The group has studied the presence and association of neurogenesis and angiogenesis in breast cancer across subtypes, at the level of protein expression data (IHC), single-cell based spatial mapping by imaging mass cytometry (IMC), and by transcriptomics and proteomics patterns at case-level. Data indicate that neurogenesis and angiogenesis are associated features and linked to aggressive breast cancer, providing support to novel treatment possibilities (Wik et al., submitted).

Data from the group have indicated that Stathmin might be a regulator of angiogenic and immunogenic responses in the microenvironment of aggressive breast cancer (Askeland et al., Sci Rep 2020). The project has been extended by single-cell based spatial mapping of Stathmin in association with immunogenic and angiogenic cell populations, searching for tissue niches that could be Stathmin dependent and applied as biomarkers and potential targets for novel treatment (Askeland et al., in preparation). Nestin, which is associated with Stathmin in breast cancer, has been linked to aggressive phenotypes and considered to be a stemness marker, although the mechanisms for this is not clear (Krüger et al., Sci Rep 2017). The role of Nestin in breast cancer is being further explored by CRISPR-based knockdown and animal models (Ardawatia et al., in preparation).

Current challenges
A major challenge in the field of deep tissue profiling is to represent the complexity and heterogeneity within malignant tumors at the proteome level. Future studies need to improve information on spatial resolution. Mapping of cancer tissues with definition of functional cellular niches will increase the precision of data for prognostic and predictive purposes in current onco-medicine.

Focus and plans for the next two years
In the Akslen group, projects will continue to explore the phenotypic diversity and complexity of breast cancer subtypes, with focus on single-cell spatial mapping and niche architecture.••

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T2

JAMES B. LORENS

Research focus
In spite of significant improvement 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 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 of 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 2021
1. *AXL is a Key Factor for Cell Plasticity and Promotes Metastasis in Pancreatic Cancer*
Single-cell RNA-sequencing revealed that AXL is highly expressed in tumor cells that have EMT. AXL deficiency extended survival, reduced primary and metastatic burden, and enhanced sensitivity to gemcitabine in murine models of pancreatic ductal adenocarcinoma (PDA). PDA in AXL-deficient mice displayed a more differentiated histology, higher nucleoside transporter expression, and a more active immune microenvironment compared with PDA in wild-type mice. Finally, the group demonstrated that AXL-positive poorly differentiated tumor cells are critical for PDA progression and metastasis, emphasizing the potential of AXL as a therapeutic target in PDA.

2. *AXL in renal carcinoma*
High AXL-expression level in tumor cells was associated with lower response rates and a trend to shorter progression-free survival following anti-PD-1 treatment in clear-cell renal cell carcinoma (ccRCC). AXL expression was strongly associated with tumor-PD-L1 expression, especially in tumors with VHL inactivation. Moreover, patients with tumors displaying concomitant PD-L1 expression and high AXL expression had the worst overall survival. In orthotopic ccRCC murine models, AXL targeting with small molecule kinase inhibitor or function-blocking antibody inhibited tumor progression. These findings propose AXL as a candidate therapeutic target in advanced ccRCC.

Current challenges
Deeper understanding of 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 plans for the next two 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. ••

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T2

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 (fibroblast) interactions.

• Stroma as a source of prognostic biomarkers.

• Development of point-of-care cancer diagnostic tools for use in resource poor settings.

Important results
To investigate the role of microRNAs in tumor-stroma (fibroblasts) interactions, the group investigated the dysregulation of miRNA in tumor stroma (fibroblasts). This study identified twelve differentially expressed miRs in stromal fibroblasts of OSCC lesions compared with normal oral mucosa (Rajthala et al., Int J Mol Sci, 2021) and it revealed that one of the significantly downregulated miRNAs in CAF, miR-204, has a tumor-suppressive function through inhibition of fibroblast migration by modulating the expression of several different motility-related molecules. The group shows for the first time that miR-204 targets integrin α11, a collagen I receptor that has been involved in cell motility and showed previously by the group to be specifically upregulated in CAFs. Furthermore, in a cohort of 169 patients with human papilloma virus (HPV)-negative primary OSCC, they showed that presence of miR-204 in the stroma at the tumor front predicted better overall survival and recurrence free survival (Rajthala et al., Cancers, 2021).

The Costea group further characterized comprehensively their head and neck cancer cohort at several levels: mutational landscape by NGS using a custom-made 31 gene panel, desmoplastic reaction, and host immune reaction. The group identified a panel of 7 genes that had a prognostic value for head and neck cancers (Dongre et al., Front. Oncol. 2021) and that presence of at least one cancer-specific mutation in any of these genes was positively associated with an aggressive type of invasive front and extensive desmoplastic stroma. Of interest, it was found that extensive stromal desmoplasia positively associated with an aggressive tumor invasion front and presence of metastasis, but surprisingly, inversely associated with a rich inflammatory infiltrate.

Oral cancer is increasing at an alarming rate, particularly in low-income countries. This urges for research into noninvasive, user-friendly diagnostic tools that can be used in limited-resource settings. The group tested and validated the feasibility of e-nose technology for detecting oral cancer in the limited-resource settings of the Sudanese population, where it offers a valuable cost-effective strategy to tackle the burden posed by OSCC (Mohamed, Healthcare, 2021).

Current challenges
The group has shown that cancer associated fibroblasts are heterogenous and involved in complex interactions 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 tumor progression and drug resistance.

Focus and plans for the next two years
The group will focus on deep characterization of fibroblast subpopulations and their interaction with cancer cells, inflammatory and endothelial cells by use of imaging mass cytometry (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. ••

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T2

CAMILLA KRAKSTAD

Research focus
The Bergen Gynecologic Cancer Research Group focuses on molecular profiling of endometrial and cervical cancers, to better understand alterations associated with cancer development and progression and with the ultimate goal to improve treatment. The group's research is based on patient samples collected over two decades with extensive clinical information available. In recent years, a special focus has been on establishing patient-derived organoid model systems for endometrial cancer alongside a continuous effort to gain knowledge on the genetic landscape of endometrial and cervical cancer.

Subprojects
During 2021, the group has continued its focus on improved diagnostics and treatment for endometrial and cervical cancer, including a large study on the genetic alterations associated with cervical cancer. To enable mechanistical studies of such findings, model systems have been developed, including patient-based organoids and orthotopic mouse models. A current focus is within radiogenomics, where the group's competences within genomics, mathematics and imaging are combined to integrate genomic and radiology data for improved pre-operative diagnostics.

Important results
Several important findings have been published during 2021. First, the group is the first to establish patient derived endometrial cancer organoids. The models were deeply characterized and compared to their donor counterparts. Models were found to be both representative for endometrial cancer, genetically stable in culture and mimic disease development when orthotopically implanted in mice. Second, the power of integrating radiologic and genetic data in a radiogenomics study of endometrial cancers was demonstrated. Unsupervised clustering of texture features from preoperative images could identify a patient subgroup with significantly worse prognosis, and distinct genetic features. In a follow-up study, the group currently investigates whether similar approaches can be valid also in cervical cancer. Third, the MOMATEC2 study is ongoing for evaluation of hormone receptors as biomarkers in endometrial cancer. As part of this study, quality of life data is collected. The first report on such data was published in 2021, with a special focus of long-term effects of chemotherapy and lymph-node staging.

Current challenges
As the incidence of endometrial cancer is expected to rise due to its tight link to obesity and high age, three main challenges are:

1. Translating genetic knowledge to better treatment.

2. Identifying specific patient sub-populations that are likely to respond to therapy.

3. Link molecular subgroups, often defined by the TCGA classification, to relevant treatment.

Focus and plans for the next two years
The group will continue to develop their molecularly defined models for endometrial cancer and use these for drug testing, functional experiments, and exploration of subtype specific genetic alterations. The group is working closely with collaborators at The Broad Institute and Dana Farber Cancer Institute, Harvard, to identify dependencies and vulnerabilities in these models. The members will expand the biomarker focus exploiting the Hyperion Imaging System and relevant biomarker-panels for both stromal and tumor components and will continue the strong focus on MOMATEC2, aiming to complete this prospective trial together with contributing centers, both nationally and internationally. ••

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T2

ELISABETH WIK

Research focus
The research group Breast Cancer of the Young – Bergen (BCY-B) was established in 2019, focusing on studies of breast cancer in women younger than 50 years of age. This group experiences more aggressive tumors and poorer survival compared to what is expected based on traditional clinico-pathologic prognostic measures. BCY-B studies age-related breast cancer biology, aiming for diagnostic biomarker development and improved prognostication for the group of young breast cancer patients – a project of high clinical relevance.

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

2. Age-dependent transcriptomic alterations in breast cancer of the young

3. Age-dependent differences in immuno-angiogenic responses in breast cancer

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

Important results
The BCY-B group is still in an early phase. Over the last years, well annotated cohorts of tissue from the BCY patients have been established, including matched primary and metastatic tissue, and strong follow-up data. One paper is submitted (Ingebriktsen et al.). Work on GATA3, FOXA1, AGR2, and TFF1 is ongoing as part of the subproject "Estrogen receptor-related biology in breast cancer of the young". Further, studies of transcriptional age-dependent alterations and molecular subtypes in metastases from breast cancer of the young, are in progress. Submission of the first paper from the BCY-B group, completion of cohort collection, and funding for one new PhD student have been achieved in 2021.

Current challenges
International studies on this patient group are limited. Clinically relevant findings from studies by the BCY-B group needs validation in external cohorts. Collaborative work is needed, and Nordic and European collaborative efforts will be initiated.

Focus and plans for the next two years
BCY-B aims to further explore the tumor microenvironment with age-related biological differences in focus. The group will also focus on response to endocrine therapy in BCY (subprojects 1 and 3). Validation studies, in both in-house and external cohorts, are planned for. Expansion of well-annotated BCY cohorts, including tissue data, is initiated. Efforts to establish international collaborations and networks are planned. ••

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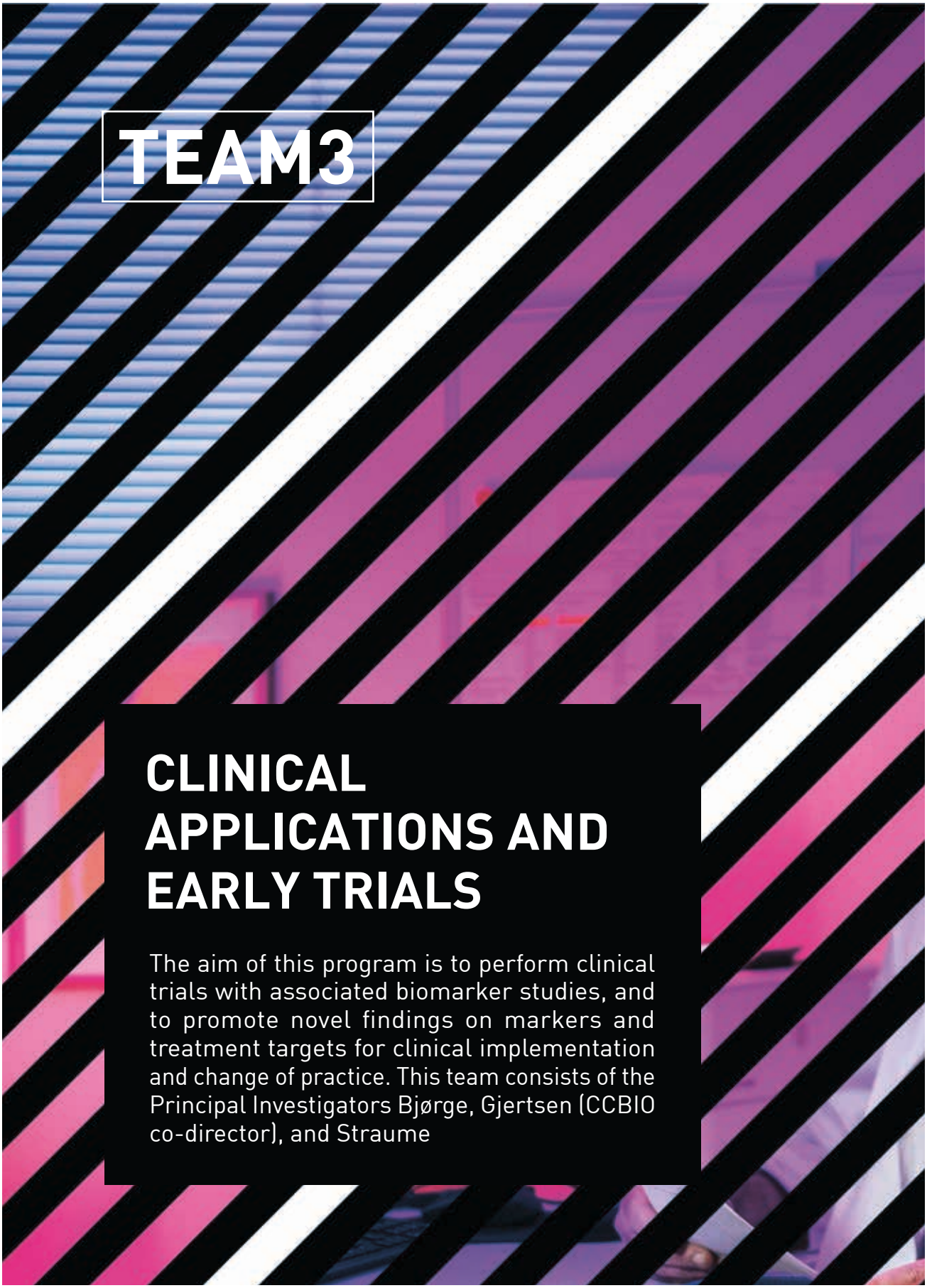

TEAM3

CLINICAL APPLICATIONS AND EARLY TRIALS

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 Bjørge, Gjertsen (CCBIO co-director), and Straume

T3

BJØRN TORE GJERTSEN

Research focus
The Gjertsen group focuses on how intracellular signal transduction is altered in cancer cells of patients treated with conventional or targeted therapy. The experimental framework is based on tumor cells collected in clinical trials, examining how signaling in tumor cells is related to therapy response. The signaling systems wire the cells and orchestrate a complex regulation of cell proliferation and cell fate. The group has chosen the transcription factor and tumor suppressor p53 as a model for a molecular integrator of cell signaling metabolism and cell stress.

Signal transduction is directly involved in leukemogenesis in 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. AML is compared with chronic myeloid leukemia (CML), characterized by a BCR-ABL1 fusion where the ABL1-part comprise a leukemogenic tyrosine kinase.

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 on response to immune therapy, and this will be examined in greater detail.

The p53 research aims to examine whether the p53 system is a ubiquitous biomarker for diagnosis and response evaluation. Ongoing work address how AXL may regulate the p53 protein in AML.

Important results
Identifying the impact of sex in prognostication of mutated receptor tyrosine kinase in AML, drawing an outline of complex biological confounders.

Current challenges
We need better biomarkers for early identification of responders in aggressive cancer. Differences in prognostication by mutations based on sex may be drawing an outline of how confounders may make precision therapy even harder to reach.

Focus and plans for the next two years
The group is preparing publications of several extensive research projects in 2022 and 2023. This includes the study of the AXL inhibitor bemcentinib in acute myeloid leukemia, a phase I/II clinical trial that was fully recruited in September 2021 with more than 80 patients in part A and B (ClinicalTrials.gov Identifier: NCT02488408). This work includes single cell immune and signaling profiling and examination of tumor cell fate.

The research will examine how signal transduction modulate the tumor suppressor p53 in myeloid leukemia. The group has shown that wild type p53 is strongly activated 2-4 hrs after start of therapy, with extensive p53 induced gene expression. How signal systems orchestrate p53 in tumor cells during therapy is not known, and whether the manifold pre-mRNA splice forms of p53 play a more important role than the multitude of p53 post-translational modifications, is not known. The connection between signaling systems and p53 will be studied in AML treated with conventional chemotherapy, the AXL inhibitor bemcentinib, or the BTK inhibitor ibrutinib, in search for a biomarker panel that may inform on therapy response. ••

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T3

ODDBJØRN STRAUME

Research focus
The main research goal is to identify predictive biomarkers in clinical cohorts. The group studies population-based patient series and clinical trials.

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

• Clinical trial: A national, multicenter, interventional study of ipilimumab in patients with unresectable or metastatic melanoma (IPI4). The goal is to identify predictive markers.

• 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.

• 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 micro-metastases can initiate tumor growth following a systemic burst of growth factors after surgery or trauma.

Important results
Some selected results from the projects above:

1: 70 patients have received treatment in the trial as of January 2022. Five regional centers include patients. After the outbreak of the COVID-19 pandemic, enrollment was significantly slowed down, but is now picking up again. The project still needs to recruit 16 more patients before the group can start reporting on safety and efficacy as well as starting to analyze candidate predictive biomarkers for response to anti-AXL targeted therapy.

2: The IPI-4 prospective trial represents the longest reported follow-up of a real-world melanoma population treated with ipilimumab and was recently published for clinical data. Results indicate safety and efficacy comparable to phase III trials and suggest that the use of ipilimumab can be based on current cost-benefit estimates. The group has now collected tissue samples from primary tumors and pre-treatment metastatic biopsies and has started preparing the material for predictive marker studies.

3: The group assessed the expression of proteins involved in regulation of stress response in a series of melanoma metastasis treated with bevacizumab monotherapy. β2-adrenergic signaling is a stress response mechanism that impacts numerous hallmarks of cancer. To the best of our knowledge, the group is the first to show the correlation between strong expression of β2-adrenergic receptor and clinical benefit from bevacizumab in melanoma.

4: The group has demonstrated an augmented stimulating effect on relapse dynamics in patients experiencing complications in the perioperative period as well as in obese patients.

Current challenges
First, the lack of reliable and robust predictive biomarkers of response to treatment for cancer is still a major challenge. Second, in most cancer types, the response to immune checkpoint inhibitors is poor, and we need to develop new strategies to increase response rates in these cancer types. Third, cancer is a systemic disease, and the majority of cancer deaths are due to metastatic disease. Thus, an increased focus on what causes escape from tumor dormancy and late metastatic relapses is warranted.

Focus and plans for the next two years
The group is currently in the process of designing a new phase 2 clinical trial in renal cell carcinoma combining cryoimmunotherapy with immune checkpoint inhibitors. Two more clinical trials are being planned. The group currently has an increasing focus on the importance of different stress responses in physiologic downregulation of the normal defense against DNA damage. Efforts to investigate the biology behind these evolutionary conserved mechanisms will be intensified. ••

GROUP MEMBERS:

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


T3
LINE
BJØRGE

Research focus
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 are being integrated into clinical trials and wider practice. The 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).

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 nor systemic metastases, a similar research program as well as a multidisciplinary team has been 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. Their two-investigator initiated early-phase clinical study is still ongoing. The last year, PhD student Shamundeeswari Anandan successfully defended her PhD thesis.

Current challenges
Based on the improved recognition of cellular and molecular diversity, a more refined personalized approach to research and clinical trials for 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. Due to the pandemic, the recruitment to the group's investigator-initiated studies has for periods been stopped temporarily. Also, late delivery of equipment has delayed the progress for many of the ongoing projects.

Focus and plans for the next two years
Biological characteristics of HGSOC and vulva cancer influence the effect of different therapies (surgery, radiotherapy, chemotherapy, targeted therapeutics), and to be able to select more individualized treatment, establishment and validation of preclinical platforms for deep-tissue profiling and drug screening, is necessary. This can be achieved through comprehensive profiling programs which are being established. Further, given the importance of surgery for both diseases, tumor targeted fluorescence-image guided surgery methodologies will be further developed. The group has the following objectives:

1. To generate unique HGSOC and vulva cancer organoid platforms

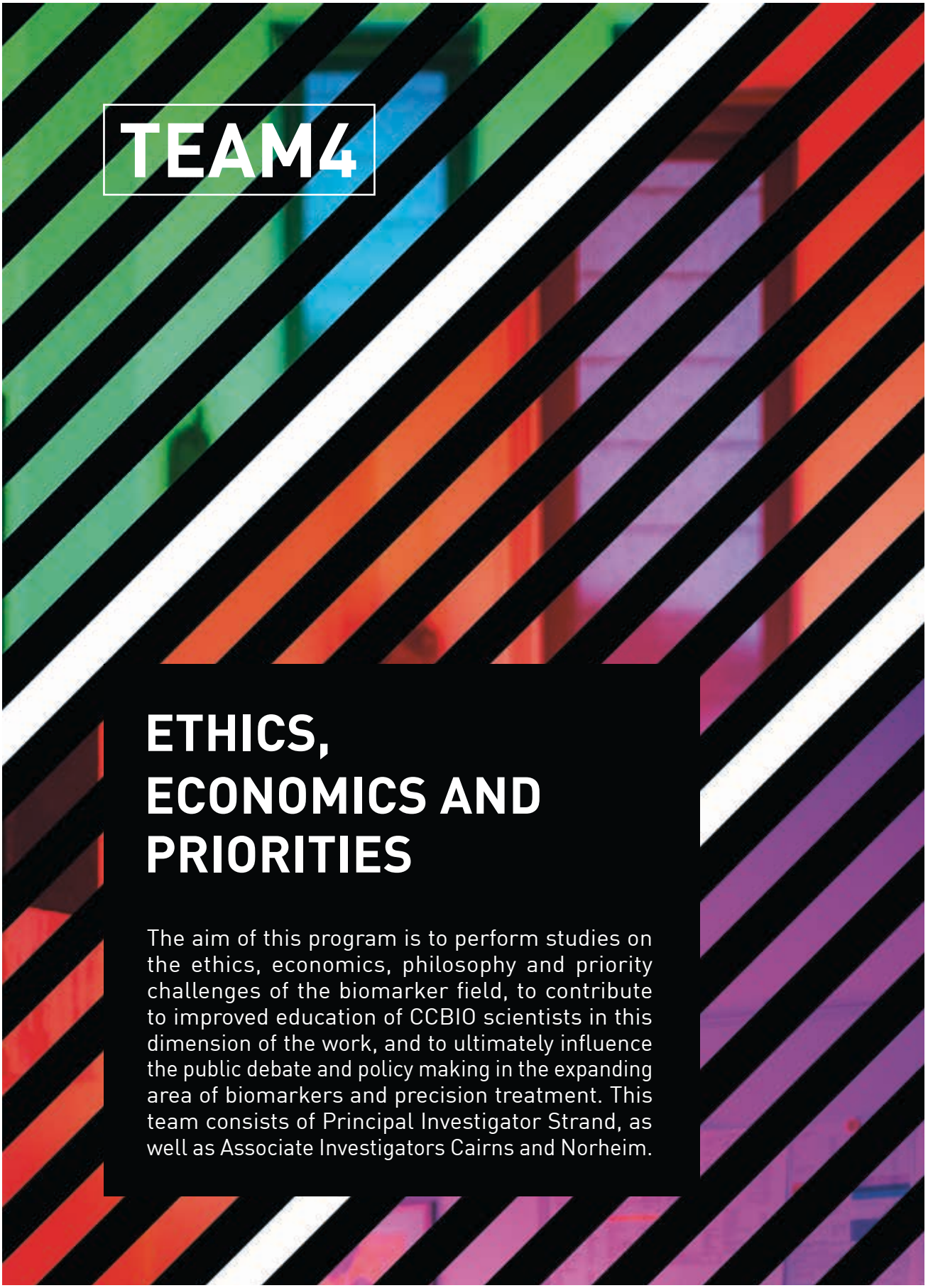
2. To integrate the use of single-cell profiling of well-defined clinical trial cohorts to define biomarkers and preclinical models (PDX models) that portray the *in vivo* activity of the study drug(s)

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

4. To identify chemoresistance-associated HGSOC subpopulations to enable precision cancer treatment. ••

GROUP MEMBERS:

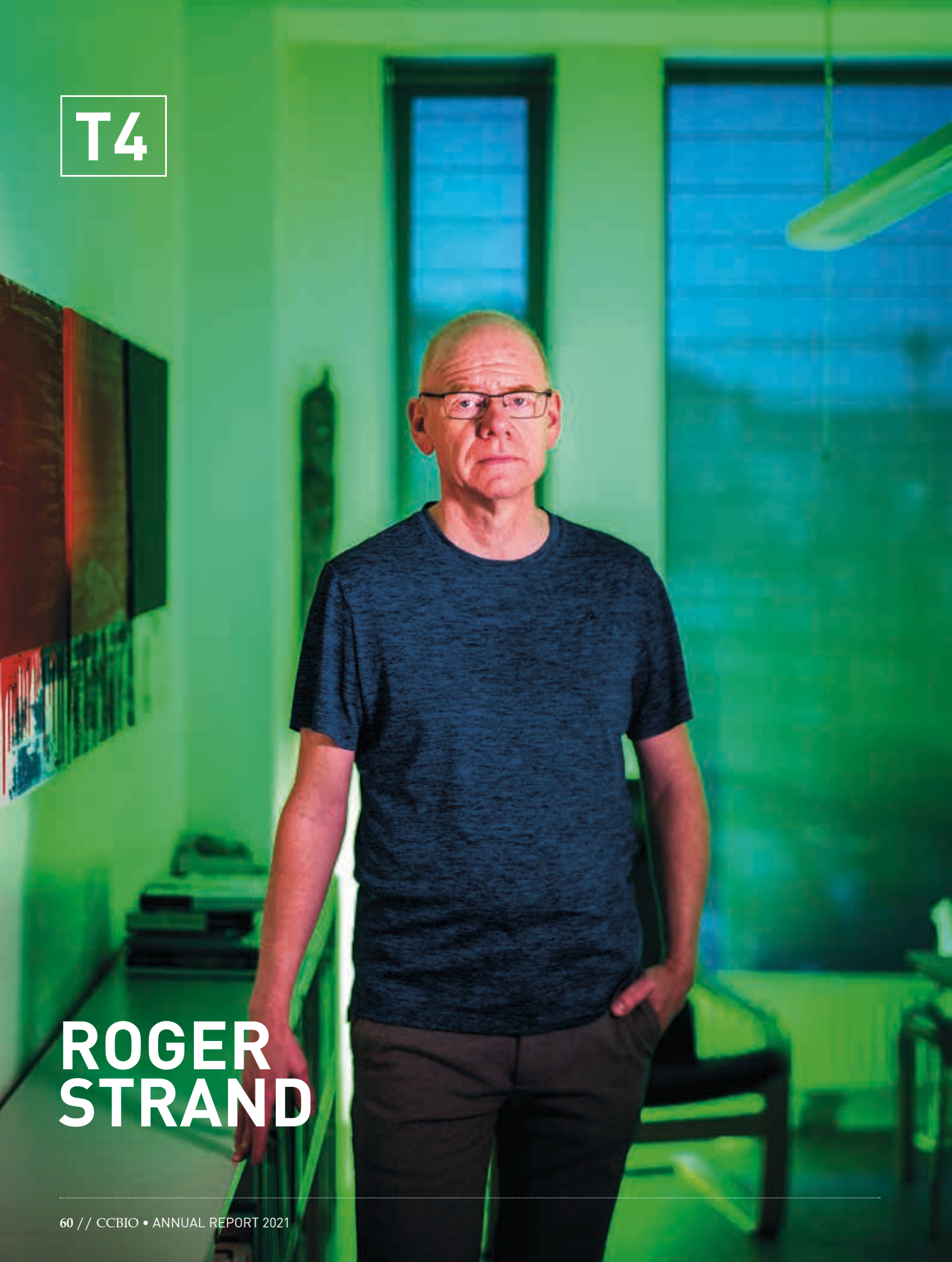
Bjørge, Line, MD, PhD, MBA, professor, group leader
Anandan, Shamundeeswari, MS, PhD candidate
Dongre, Harsh, MS, PhD, postdoc
Enge, Elisabeth, study nurse
Fosse, Vibeke, DVM, veterinarian
Gissum, Karen Rosnes, MS, PhD candidate
Gjerde, Christiane Helgestad, MD, PhD candidate
Kleinmanns, Katrin, MS,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



TEAM4

ETHICS, ECONOMICS AND PRIORITIES

The aim of this program is to perform studies on the ethics, economics, philosophy 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 the public debate and policy making in the expanding area of biomarkers and precision treatment. This team consists of Principal Investigator Strand, as well as Associate Investigators Cairns and Norheim.


T4
ROGER
STRAND

Research focus
Strand's group performs research on the ethical, legal and societal aspects (ELSA) of CCBIO's research, distinguishing between two interrelated goals:

1. A better understanding of the developments, expectations, and imaginaries of personalized and precision cancer medicine, including its political economy and ethical and social issues.

2. A better integration of this understanding into practices of "responsible cancer research" in the sense of RRI (Responsible Research and Innovation).

Projects
The ELSA group of CCBIO is a small-scale operation that can be seen as one project. They interact and are tightly linked, however, to similar ongoing 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 2021, the group reached an important milestone, namely submission of the interdisciplinary research anthology "Precision Oncology and Cancer Biomarkers: Issues at Stake and Matters of Concern", edited by Anne Bremer and Roger Strand. Later in 2021, the anthology was accepted for publication by Springer Publishing.

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 2021, the key focus was interdisciplinary analysis of the sociotechnical imaginaries of personalized and precision cancer medicine, resulting in the above mentioned 16-chapter research anthology. In general, it can be said that the group has searched for *re-framings* of cancer, and such re-framings have been presented in the anthology, drawing on complexity theory, medical philosophy, Daoist philosophy, science and technology studies, post-normal science, health technology assessment, et cetera. Strand believes this project can be seen as, if not finalized, at least reaching its final stage.

Current challenges
The challenge of practical relevance remains, and also the challenge of dissemination of our research results, which have the quite narrow view of precision oncology and cancer biomarkers and at the same time require an adequate level of scholarship for their uptake.

Focus and plans for the next two years
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. It is also important for the group to take part in the overall endeavor for CCBIO to summarize, analyze and synthesize the accumulated scientific progress that CCBIO has led to over its 10 years of existence.••

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

T4

OLE FRITHJOF NORHEIM

Research focus
The Bergen Centre for Ethics and Priority Setting (BCEPS) was established in 2019 with funding from the Bill & Melinda Gates Foundation, Trond Mohn Foundation, Norad and the University of Bergen. BCEPS has continued its expansion with activities in Ethiopia, Zanzibar, Malawi, Nepal, Ghana, Tanzania and Africa CDC. The center is also a finalist for a new Centre of Excellence grant from the Norwegian Research Council. BCEPS continues to work on priority setting challenges in Norway. The collaboration with CCBIO on cancer biomarkers, precision medicine and fair priority setting is central to this aim.

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 hopefully improve health care priority setting. How is our ethical thinking about treating people as equals challenged when biomarkers and other individual characteristics stratify patients into smaller and smaller sub-groups, with only some being offered new and potentially life-saving treatments?

Subprojects
The PhD project investigating how cancer biomarkers inform treatment recommendations for new and expensive cancer drugs was completed in 2021. In the first PhD defense open to the public since the corona pandemic started, candidate Eirik Joakim Tranvåg successfully defended his thesis on September 24.

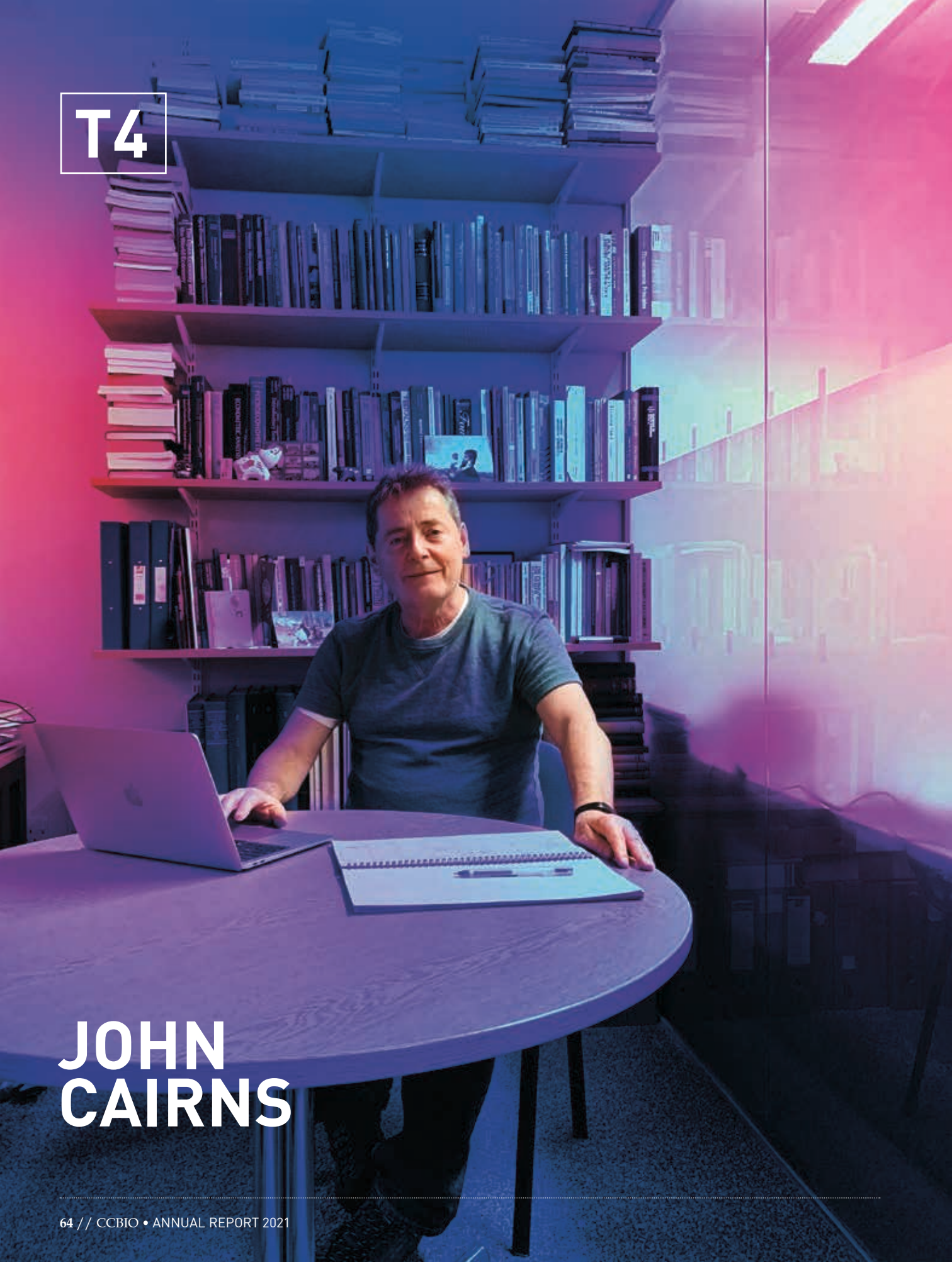
Important results
One of the articles in the dissertation was published in BMC Medical Ethics in May. In "Precision medicine and the principle of equal treatment: a conjoint analysis" Tranvåg and co-authors surveyed Norwegian cancer doctors' stated preferences towards priority setting between cancer patients and found that biomarker status was perceived as relevant in the decisions. Another part of the dissertation will be published in the forthcoming Springer series book by CCBIO's ELSA team. In a book chapter, Tranvåg and Roger Strand discuss important ethical and societal perspectives on priority setting and personalized medicine.

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

Focus and plans for the next two years
The team will continue work on priority setting at both clinical- and policy levels. The last article from Tranvåg's dissertation will be published in 2022. 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. Norheim aims to continue the good dialogue and exchanges with other CCBIO researchers and clinicians. • •

GROUP MEMBERS:

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



T4

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
Jiyeon Kang is now nearing the completion of her PhD entitled "Improving economic evaluation and decision-making for oncology drugs using real-world data". She has built a unique database of nearly 200 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. Her data extraction protocol was recently published. A number of research papers are at an advanced stage. These include a detailed account of how real-world data has been used to inform decision making, a paper testing a series of hypotheses regarding the use and acceptability of real-world data in NICE appraisals, an analysis comparing the use of data in appraisals of targeted cancer therapies and non-targeted cancer therapies, and a timely study of the first nineteen medicines to exit the Cancer Drugs Fund.

Jiyeon Kang and John Cairns each contributed chapters to the forthcoming volume "Precision Oncology and Cancer Biomarkers" (edited by Bremer and Strand). The former examines the use of real-world data to assess targeted cancer therapies, and the latter highlights differences in the assessment of the cost-effectiveness of checkpoint inhibitors and targeted therapies for treating non-small cell lung cancer.

Important results
The identification and analysis of the limited role played by real-world data in actual appraisals of oncology medicines, in contrast to the widespread enthusiasm for increased use of real-world data is an important output from this research. Also, the group is making progress in understanding how decision-making processes regarding the adoption of new health technologies and the economic evaluations of cancer drugs interact.

Current challenges
The development of the methods of technology appraisal to facilitate the production of robust estimates of cost-effectiveness around the time new products are launched remains a major challenge.

Focus and plans for the next two 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, FRCP,
professor, associate investigator, group leader
Gabrielsen, Tommy Staahl, MA, PhD, professor
Kang, Jiyeon PharmD, MS, PhD candidate
Luís, Ana Beatriz Mateus D'Avó, MA,
PhD candidate
Riise, Julie, MA, PhD, associate professor

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 microenvironments, 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 in Jonassen's group is working on developing and applying methods for analysis of various omics and single cell data generated by the partners. In this project, the group applies systems biology modeling and machine learning approaches aimed at predicting outcome and aid selection of treatment for individual patients, using a set of different experimental model systems and piloting clinical trials. For example, in a collaborative project with the Gjertsen group, results are promising, identifying single cell markers correlated with leukemia patients' treatment response and survival. Another postdoc associated with CCBIO is working on development and use of methods to exploit the Hyperion imaging technology to the study of tumor microenvironment interactions. Pipelines including identification and annotation of individual cells have been established and current work includes analyzing a data set generated in the Akslen group encompassing a sample of breast tumors with associated outcome data. Jonassen expects a number of publications to result from the work in the coming year.

Important results
Relevant to Jonassen's work in CCBIO, he published (in BMC Bioinformatics) in 2020 a flexible and versatile workflow for RNAseq data analysis, (in BMC Genomics) a comprehensive study comparing alternative approaches for characterizing DNA copy number variants, and (in Acta Neuropathologica Communications) a study showing that expression signatures seen in Parkinson are mainly driven by cell type composition. The latter work has relevance in analysis of leukemia and solid tumor data analysis where the group is now using single cell data to be able to better dissect changes in gene expression and relations to cell types and tumor microenvironments.

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 plans for the next two years
Presently, the group is seeing promising results analyzing both the CYTOF and the Hyperion data. More work is needed to be able to fully exploit the data and to use it together with other data modalities on the same patients. To support this work, Jonassen and collaborators are currently preparing a new EraPerMed application following up the work started in the AML_PM project. The group will explore if some of the work, including that started on analysis of Hyperion data, can in part be linked with new institutional and medical faculty initiatives on artificial intelligence. ••

GROUP MEMBERS:

Jonassen, Inge, MS, PhD, professor, associate investigator, group leader
Ehsani, Rezvan, PhD, postdoc
Kleftogiannis, Dimitrios, PhD, postdoc

STRATEGIC ADVICE

ROLF K. REED

Professor Rolf K. Reed stepped down as PI during 2018 and entered into a role as strategic adviser to CCBIO for the second term. His commitment towards CCBIO is the same as when he was PI in parallel with being head of the Department of Biomedicine. Reed still has students and research activities under the CCBIO umbrella. He is currently affiliated to the Lorens group at the Department of Biomedicine. Among these are Hilde Ytre-Hauge Smeland who defended her PhD in 2021, in a project investigating the role of integrin $\alpha 11\beta 1$ in breast cancer and its potential as a cancer biomarker. The project is a collaboration where Professors Stuhr, Akslen and Gullberg also are part of the supervisory team.

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 benefits from a long experience in 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 is brought into the longtime strategic planning at CCBIO, both for the remaining duration of the center 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 2021 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 was member of the Biosciences Panel of European Academies of Sciences Advisory Council as delegate for The Norwegian Academy of Science and Letters.

Research activities

The research activities are currently focused on a collaboration on PDX-models with Professor Linda Stuhr. Another ongoing project is the turnover of potential biomarker proteins, such as sAXL in the intact organism to understand how it is turned over by transport through the circulatory-interstitial-lymphatic system. The project is performed together with Professors Lorens and Tenstad at the Department of Biomedicine. However, as most other research projects, these have been delayed due to the corona measures. ••

INTERNATIONAL FACULTY

The CCBIO International Faculty consists of internationally high-ranking scientists within relevant fields of cancer research. They mostly have 10% adjunct professor or researcher positions at CCBIO. 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. This has successfully strengthened CCBIO's collaborative networks as well as its research. Another important aim has been to enable CCBIO's Research School to organize research-based courses at the highest level and to enable co-supervision and exchange of PhD candidates and postdoctoral fellows. In 2021, CCBIO's International Faculty numbered 15 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 scientific part 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. In 2021, he founded the Advisory Board on Cancer, Infertility and Pregnancy (ABCIP, www.AB-CIP.org) 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. He is co-PI of the CoNteSSa-NEOCON study that explores the potential to preserve fertility in young women with cervical cancer. In 2022, he will also focus on the EUGENIE study in endometrial cancer, that aims to link surgical stage to the molecular classification.

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 radio-genomic 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 during 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 co-director of the CNRS-European Associated Laboratory (Nancy University, France) from 2010-2018. He was awarded the prestigious fellowship from the Breast Cancer Campaign in 2012. He is head of the P53 Isoforms and Virus Laboratory at the School of Medicine, Dundee University since 2005.

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. P53 isoforms promote genome reprogramming and induce iPSC. 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). He has made these antibodies 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-supervised 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 the AXL receptor kinase inhibitor developed at BerGenBio and CCBIO (BGB324). Hajjar successfully completed his PhD in December 2020, and several publications are expected in 2022.

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 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.

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.

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, he 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. Professor Gabra 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 a new role as Chief Medical Officer of BerGenBio in Oxford and Bergen, offering an opportunity to work with the BerGenBio team to drive forward AXL targeted clinical development. In 2021, he co-founded and took on the role of Chief Scientific Officer of Papyrus Therapeutics, an evolving preclinical stage biotech company developing tumor suppressor therapies based on OPCML and the IgLON family. Working with Professor Jim Lorens in Bergen, Professor Gabra and Professor Lorens are developing novel agents that mediate IgLON/OPCML tumor suppressor effects clinically. 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 Papyrus Therapeutics, working with Professor Lorens, Gabra intends to foster deeper collaborations with CCBIO, particularly around translational and clinical research for AXL targeted therapy and OPCML/IgLON based tumor suppressor therapies.

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 research 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. Recently, their work appeared on the cover of Nature Aging showing that age-dependent cytokeratin changes in luminal cells happen at a much accelerated rate in pathologically normal breast tissues of women who are germline carriers of pathogenic variants of BRCA1, BRCA2, or PALB2 genes (Shalabi et al.). They reported in Cancer Prevention Research a breast specific biological clock that was used to estimate that the biological age of epithelia in these high-risk women is accelerated by as much as four decades compared to their chronological age (Miyano et al.). This collaboration continues to explore the role of cytokeratins in aging and cancer susceptibility. Second, they reported in Integrative Biology (Ertsaas 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 awarded John Black Associate Professor of Prostate Cancer. In late 2021, he became Acting 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 supported 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 in Norway, Finland and the UK.

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 assessed transcript expression in archival samples and associated transcript expression with clinical outcome. They have also utilized single-cell sequencing data from pre-clinical cancer models to derive clinically relevant signatures of treatment response and outcome and have most recently utilized spatial transcriptomic data to identify clonal cancer hierarchies in prostate tissue samples. In striving to improve the early detection of clinically significant prostate cancers, they have continued to refine polygenic hazard scores to account for a wider range of ethnicities and ancestries. Biologically, Mills and collaborators continue to focus on the effects of androgen receptor (AR) signaling on prostate cancer and have uncovered novel regulatory crosstalk between the AR and membrane trafficking in the secretory pathway (Golgi-endoplasmic reticulum) mediated by calmodulin-dependent kinase 2 (CAMKK2). They have also identified impacts of the AR on lipid metabolism and the pentose phosphate pathway. Transcriptionally, they have shown cyclin-dependent kinase 9 is an important regulator of splicing in prostate cancer cells which supports the expression of an androgen-independent splice variant of the AR (AR-V7) associated with impaired responses in Abiraterone and other clinically approved AR-targeted therapies. Finally, Mills and collaborators have initiated a research project to apply light sheet microscopy to human tumor samples with the aim of generating 3D/high-depth imaging data on biopsy samples to enhance the histopathological scoring of prostate cancer and of generating image-based correlates of transcriptomic and other molecular data.

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 groundbreaking 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 has 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. Klaus Pantel has also initiated the inclusion of CCBIO´s researchers into the program of his second ERC Advanced Investigator grant INJURMET, focused on the question whether diagnostic biopsies or surgery can contribute to the dissemination of tumor cells and whether this dissemination is relevant to the development of metastatic relapse.

JEFFREY POLLARD

Professor Pollard graduated with a first-class special honors degree in Zoology from Sheffield University followed by a PhD at Imperial Cancer Research Fund (now CRUK) in London. He spent a post-doctoral period at Ontario Cancer Institute in Toronto and thereafter took a faculty position at King's College University of London. In 1988, he joined the Albert Einstein College of Medicine in New York where he worked for 24 years. At the Albert Einstein College of Medicine, Professor Pollard was the Louis Goldstein Swann Chair in Women's Health, Deputy Director of the NCI funded Cancer Center, and Director of the NIH funded Center for the Study of Reproductive Biology and Women's Health. He joined the University of Edinburgh in 2012 as Director of the Medical Research Council Centre for Reproductive Health. In Edinburgh he is Professor of Resilience Biology in the College of Medicine and Veterinary Medicine.

Professor Pollard is a Fellow of the Royal Society of Edinburgh, Fellow of the Royal Society of Biology, Fellow of the Academy of Medical Sciences, and a Fellow of the American Association for

the Advancement of Sciences. He has published over 285 papers and edited several books/journal issues. He has an H-index of 110.

Professor Pollard pioneered studies on the role of macrophages in development and tumor progression. His lab was the first to demonstrate that tumor associated macrophages (TAMs) promote tumor progression and malignancy. His work has focused upon mechanisms behind these pro-tumoral actions of TAMs with a particular emphasis on metastatic disease. For these studies he was awarded the American Cancer Society Medal of Honor in basic sciences for his work in tumor immunology in 2010.

Current studies emphasize translation of mouse studies to humans, in breast, ovarian, endometrial and brain cancer. Scientifically the focus is on understanding the immunosuppressive role of macrophages towards cytotoxic T and NK cells, particularly in the context of human cancers. Studies include spatial mapping of the tumor microenvironment and its immune components to predict clinical outcomes and to develop novel therapeutics. His lab has developed new computational and imaging methods to achieve this aim. His lab also studies functions of TAMs using induced pluripotent stem cell derived human macrophages and genetic analysis in mouse models of cancer.

In 2020, Professor Pollard founded an immuno-oncology company "Macomics" dedicated to translating basic science to clinical efficacy in cancer. Professor Pollard's lab is also the UK representative on the COST pan-European network Mye-info bank on myeloid cell biology to harmonize large data sets through integrating biobanks with genomic, proteomic and transcriptomic data by computational biology.

Professor Pollard intends to develop collaborations with members of CCBIO through advising on their programs in anti-macrophage therapies particularly through anti-CSF1R therapeutics. In addition, he has developed many methods for analysis of macrophage phenotypes within tumor tissue with the intent on using these to stratify patients for therapy. The CCBIO archives will be an invaluable resource for these studies as well as the clinical translational studies performed at CCBIO. He will collaborate broadly, and from the outset with Professors Bjørn Tore Gjertsen, Lars A. Akslen and Line Bjørge.

CARINA STRELL

Carina Strell has a PhD in tumor biology from the University of Witten-Herdecke in Germany, and moved to Stockholm, Sweden in 2010 for postdoctoral studies at Karolinska Institute with Professor Arne Östman, to gain insights into translational cancer research, and work on tumor-stroma interactions in early breast cancer (DCIS). From 2016 throughout 2018, she was a researcher at the Science for Life Laboratory with Professor Mats Nilsson where she worked with the *in situ* sequencing technique to map mutations in breast cancer tissue, in collaboration with Lucy Yates at the Wellcome Sanger Institute (UK). Since 2019, she has been at Uppsala University, Sweden with the Experimental Pathology group of pathologist Professor Patrick Micke, where she has been leading a small research team on early breast cancer. She became an associate professor in 2020.

Carina Strell received in December 2021 a Trond Mohn Foundation starting grant for her project Understanding Early Breast Cancer Evolution in Space and Time (EvoMaps). Strell has a long-term collaboration with the Akslen group, and her project will be embedded at CCBIO, commencing in Bergen in 2022. She aims to establish a competitive research group within the field of early breast cancer, investigating the biological mechanisms behind why some women experience recurrent and/or treatment resistant disease while others do not. The hypothesis is that breast cancer progression and therapy response is not only dependent on the tumor cells alone, but also on the surrounding tissue microenvironment. Through adaptation of the *in situ* sequencing technique to the Hyperion Imaging System at CCBIO, Strell will perform a systematic exploration of the genetic properties of tumor cells in relation to their surrounding microenvironment over the course of disease progression and the development of treatment resistance. The overall aim of this project is to uncover and map new mechanisms of early breast cancer evolution, and to improve current diagnostic tools for breast cancer patients, reduce the treatment burden for women with early-stage breast cancer and thus improve their quality of life and spare them treatment related comorbidities.

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 and focuses on how tumors develop into the different intrinsic molecular subtypes. Her main research interests are DCIS and risk for progression to invasive disease and the role of FGFR signaling in hormone receptor positive breast cancer. 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 the importance of the tumor microenvironment for tumor progression. Tumor growth is influenced at all stages of development by the surrounding tissues, the cells of the immune system, circulating particles and even the microbiome. Recently, Sørlie has started research on endometrial cancer and with that, initiated a collaboration with Camilla Krakstad to identify blood-based predictive markers for tumor progression and response to therapy.

JEAN PAUL THIERY

Professor Jean Paul Thiery is a high-ranking international researcher currently located in China, working as a senior research fellow at the Guangzhou Laboratory. He held the position of director of research at the Centre National de la Recherche Scientifique (CNRS), Paris, until 2010. From 1995 to 2003, Jean Paul Thiery 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 from 2003 to 2006. 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 remained research director at IMCB A*STAR, senior principal investigator at the Cancer Science Institute and 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 was also a distinguished visiting professor at the Li Ka Shing Faculty of Medicine of Hong Kong University.

Professor Thiery has made seminal contributions in cell adhesion, cell migration, morphogenesis, and cancer, publishing more than 500 peer-reviewed articles in different areas of the life sciences (h-index above 120). 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 mechano-sensing and has contributed revisiting the origin of the mesectoderm, with findings that suggest the mesectoderm and the neural crest come from two distinct territories in the ectoderm.

Jean Paul Thiery characterized a murine mammary stem cell, leading 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. Jean Paul Thiery co-discovered important activating point mutations in FGFR3 in bladder carcinoma, now considered the best prognostic marker for superficial tumors. He has 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 to detect bladder cancer, and he is 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.

Jean Paul Thiery is currently collaborating with Jim Lorens and Agnete Engelsen to unravel mechanisms driving immune escape in solid tumors. He explores the role of epithelial mesenchymal transition in carcinoma in the formation of defective immunological synapses. 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 S. 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 block metastatic dissemination of human tumors. Dr. Watnick's group has 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 since 2017 been coordinating the VBP's part of the CCBIO-INTPART program, engaging actively in teaching at CCBIO courses and at the CCBIO Scientific Writing & Communication Seminar.

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 microenvironment with special focus on tumor associated fibroblasts and their role in cancer progression. Professor Östman was vice-coordinator of STRATCAN, a government funded initiative for development of excellent cancer research at KI (2010-2018) 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.

Through his international faculty position at CCBIO, Östman has since 2015 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. In this area, collaborative studies with Akslen have led to patent applications and ongoing commercial development of findings. An ongoing 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 outside of Bergen, gathering Scandinavian tumor pathologists. The initiative has since then, apart from 2020, been followed by annual meetings. The upcoming SCANPATH 2022 meeting will again be held in Bergen.

Östman has contributed to both editions of the Springer-published volumes "Biomarkers of the Tumor Microenvironment: Basic Studies and Practical Applications", edited by Akslen and Watnick (2nd edition in press, 2022). ••

CCBIO
RESEARCH SCHOOL
FOR CANCER STUDIES

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 ethical, legal and societal aspects of cancer research and treatment. The RSCS also seeks to forward flexible forms of international exchange and mobility. The RSCS has in the last years expanded its activities considerably under the leadership of Elisabeth Wik, and now has 12 credit giving courses and a broad range of other activities. 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.

All CCBIO courses and most activities are open to researchers on all levels – from the youngest students to senior researchers and faculty. CCBIO regards the open policy as an important measure to achieve a high degree of knowledge transfer. The digital solutions have expanded on this by allowing for international participation, which has been well received, in particular by other Nordic universities. This encourages more international networking and collaboration. As part of this open policy strategy, the RSCS offers participants to choose between receiving ECTS or attending 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.

When inviting speakers for lectures and seminars, CCBIO normally uses the opportunity for both students and researchers on all levels of seniority 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. The RSCS has continued its educational activities during the pandemic and provided possibilities for digital course attendance. During 2021, the RSCS also expanded its course portfolio in collaboration with the research school at Neuro-SysMed, a center for clinical treatment research on neurological

diseases. The new courses CCBIONEUR910 Patient and Public Involvement in Medical and Health Research, CCBIONEUR911 Clinical Trials, and CCBIONEUR912 Health Innovation, fit perfectly into the RSCS's existing course activities.

In 2021, CCBIO held the courses that run continuously (CCBIO901 and CCBIO902), as well as CCBIO908 in April, BMED904 in June, CCBIO903 in September-October, CCBIONEUR911 in September-October, CCBIONEUR910 in November, and CCBIONEUR912 in November-December. You can read more about these activities in separate paragraphs below. For 2022, the RSCS plans to run CCBIO901 and CCBIO902 continuously as well as CCBIO906 (February), CCBIO904 (April), CCBIO908 (May), CCBIO905 (fall term) and CCBIO907 (fall term). For all courses, we seek to improve and expand on pedagogic methods, e.g., by including inspirational lectures by successful innovators (CCBIONEUR912), mixed onsite and online participation (several courses) and also integrating patient user groups directly in the teaching (CCBIONEUR910).

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 activities are described in detail in separate chapters.

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, opportunities and limitations of their research, and anchor it in broader ethical, legal, societal, economic, and political contexts. The core of the course is structured around the two books edited by Anne Bremer and Roger Strand: "Cancer Biomarkers: Ethics, Economics and Society" (2017), and "Precision Oncology and Cancer Biomarkers: Issues at Stake and Matters of Concern" (upcoming 2022, Springer). CCBIO903 aims to address several key questions:

• What are the promises, limitations, and consequences of the "imaginary" of precision oncology?

• What are the opportunities and limits of biomarkers, and what is a "good enough" cancer biomarker in that context?

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

• In a highly medicalized culture, what does a "good life" look like for (future) cancer patients? What does it mean, to be in "good health"?

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

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

• How can economic models help guide health care resource allocation? Is it at all possible to assess the cost-effectiveness of cancer biomarkers?

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 has from the outset been highly interdisciplinary with Roger Strand from philosophy of science, Anne Bremer from science and technology studies and John Cairns from health economics. In 2021, CCBIO903 had the pleasure of welcoming Professor Marta Bertolaso, who co-designed new elements to the course and introduced the participants to the philosophy of cancer and to emerging epistemological issues in cancer research as well as the complexity of cancer. In addition, several guest lecturers were invited to share their perspectives across disciplines ranging from oncology, philosophy of medicine, economics, media studies and ethics of prioritization in health care.

The course has been held six 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 2021, the first week of CCBIO903 was held in September, and the second week in October. The participants came from a great variety of backgrounds, ranging from medical and clinical science to health economics and tissue engineering.

CCBIO903 is organized and executed by Roger Strand, John Cairns and Anne Bremer.

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 and 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.

The last CCBIO904 took place May 25-27, 2020, as 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 Norway and the other Nordic countries, elsewhere in Europe and even from California.

The organizers, at the time 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. 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 the pandemic.

Oddbjørn Straume has the academic responsibility and Reidun Kopperud is the course coordinator. The next course will be in April 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 focuses on basic molecular mechanisms pertaining to the biological role of the extracellular matrix, and runs over five days every second year, including lectures from local researchers and several internationally well-known scientists within the field of matrix biology. In June 2021, the course was combined with a DIKU summer school in fibrosis in that is part of the MOTIF-network. Due the pandemic, the course consisted of online presentations of all lectures and video demonstrations of practical lab work.

19 participants attended the June 2021 course. Attending students were from Bergen and other cities in Norway, Sweden, Denmark, and Finland. Three lecture highlights included speakers Ritva Heljasvaara (Oulu, Finland), 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 online for the rest of the participants. Microscopy of integrin-tagged cells, cell cultures in 3D collagen matrices, spheroid formation and traction force microscopy 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.

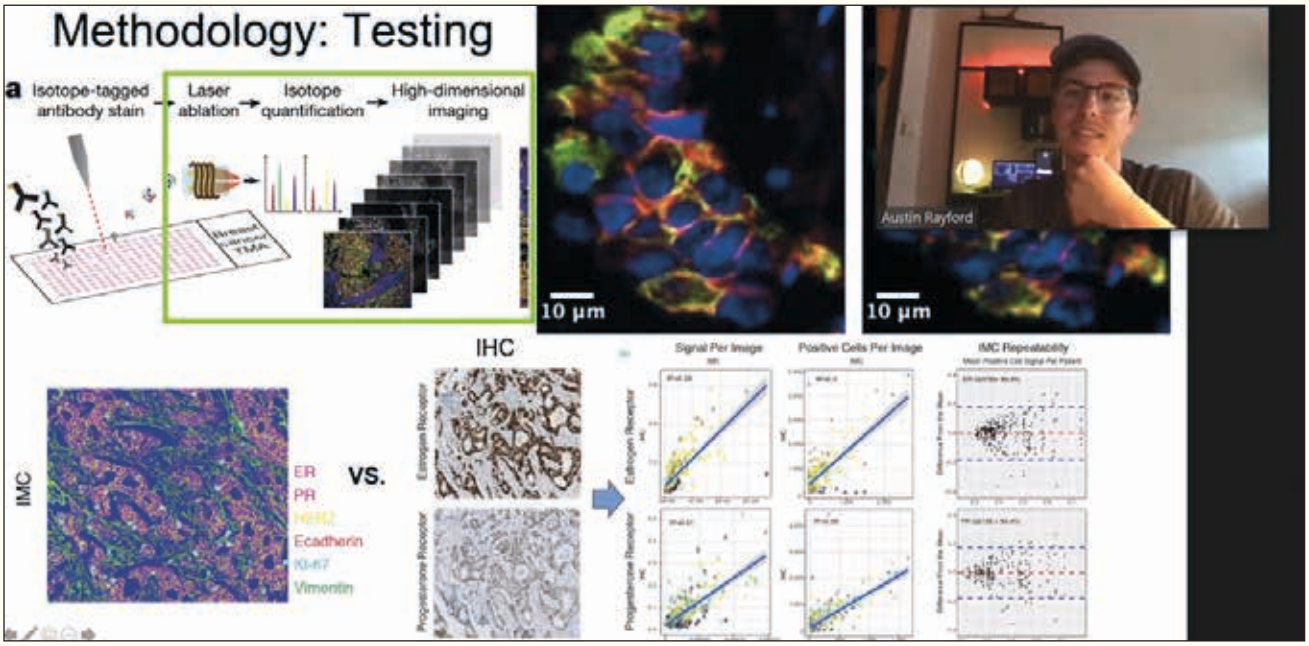
The next course will be in June 2023, covering various aspects of extracellular matrix (ECM) biology, including the structure and function of the main classes of ECM molecules, the composition of the ECM in different tissues, and cellular receptors for ECM molecules and their signaling. A recurring theme will be the roles of the various ECM molecules and their functions in health and disease as well as the role of cancer associated fibroblasts in cancer and ECM. In addition to local experts, lecturers include a range of international experts in the field. 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 biobanking. The course was established in 2015 and was last held October 27-29, 2020, then on a digital platform. 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 opting 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 reflected 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 fall 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. It was last held February 20-21, 2020 with 40 enlisted students, in large part local, but also from Oslo, Sweden, Denmark, Austria, Finland and even from Tanzania. This was before the pandemic, with on-site participation only.

Ola Myklebost had the academic responsibility from 2017 to 2020. The next course will run in February 2022, with Liv Cecilie Vestrheim Thomsen and Erling Høivik as academic responsible and Rebecca Nguyen as the course coordinator.

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. As of 2020, the course also introduced important soft skills 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.

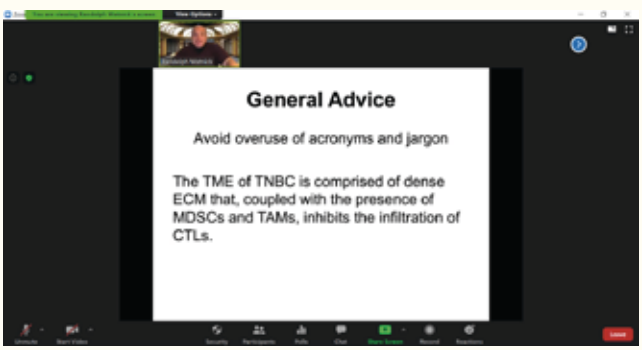
CCBIO907 was held for the first time in 2018. The last course was held September 21, October 2 and October 9, 2020, through a digital platform due to the pandemic. Digital participation boosted attendance, and 96 students and researchers took part, their affiliation ranging from Bergen to all over Norway, 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 2 ECTS adaptation of a former non-credit-giving course that is 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 first run in December 2017 and again in May 2019, and digitally for the first time in June 2020. The course was also in 2021 held digitally on April 12 and 15. Registration was then split between students wanting ECTS, and attendees participating for professional update only. 85 students attended – from CCBIO and other programs and research groups at UiB, and from other institutions in Norway, the Nordic countries, and even a few students from other continents. 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 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.

CCBIO's academically responsible in 2021 was Elisabeth Wik, with Vandana Ardawatia and Harsh Dongre as coordinators. The next course will be in May 2022.

CCBIONEUR910 – Patient and Public Involvement in Medical and Health Research

CCBIONEUR910 is a brand-new 2 ECTS course in a collaboration between Neuro-SysMed and CCBIO, aiming to create a platform for competence development and networking across professional- and user roles, facilitating communication and sharing of experience from multiple perspectives. Furthermore, the course intends to stimulate increased user participation in research trials by presenting methods for putting user involvement into practice. The main objective is to develop the participants' capacity to assess and convey the value of patient and public involvement in general, as well as promoting productive user involvement in participants' research projects.

The course spanned over three days, November 3-5, 2021, and encompassed a broad spectrum of national and international lectures from researcher and user organizations, professional users and health care employees assigned to specific user representation tasks. Challenges were addressed from both researcher- and user representative perspectives, and specific advice as well as professional and personal opinions were shared. The atmosphere during the course reflected open-mindedness and an overall pragmatic attitude to find common denominators and move forward in the heterogeneous meadow of user representation in medical research.

Simon Denegri, UK nestor and an expert on public involvement in biomedical and health research, gave a talk on patient and public involvement in a historic perspective, and provided an overview on where PPI is internationally, from involvement to co-production. Linn Merete Hefte Bæra (UKOM, The Norwegian Healthcare Investigation Board) discussed the role of experience competence and local user committees. Anne Rita Øksengard (National Association

for Public Health) dove deep into the user participation, who the user contributors are and how user participation can strengthen research. Kari Tove Elvebakken (Department of Administration and Organization Theory) gave a critical perspective on user participation in health research. Nina T. Grytten (Neuro-SysMed) and Hilde Norborg presented user participation from a researcher's perspective, including information about EUPATI Norway. John Anker Henrik Zwart (Oslo University Hospital and the University of Oslo) gave an overview of research on user participation in research and the benefits of user participation, and how it works in practice. Gina Barstad (The Norwegian Cancer Society) talked about how to recruit user collaborators in research, and Tone Skår presented *MED.hjelper*, a users' guide to participation in clinical trials. CEO of Helse Bergen Eivind Hansen explained the assignment from the health authorities and hospital management regarding user participation. Gry Lien (User Council N-SM / Alltid Litt Sterkere) and Jeanette Hoel (Rheumatism Association) shared experiences from user participants and cases where user participation made a difference. Laila Yvonne Norvoll (Section for Research and Innovation, Helse Bergen) explained how researchers involve user collaborators in clinical research. Thorleif M. Lunde from Eitri, the new medical incubator at UIB/Helse Bergen where the course took place, discussed the importance of the users in the new medical incubator. Sameline Grimsgaard from NorCRIN (Norwegian Clinical Research Infrastructure Network) presented the NorCRIN AP14 User participation program. Bettina Husebø and Rune Samdal (UiB, SEFAS) discussed what we have learned from each other. Roger Strand (CCBIO, Centre for the Study of the Sciences and the Humanities, UiB) presented power transfer and ethics: User participation in a societal perspective. Tor Jacob Moe (Fana Psychotherapy Center) discussed whether user participation can create health anxiety and performance anxiety. The program also included international perspectives in the talk "Public involvement in research using creative and inclusive practices: Planet DIVOC-91" by Bella Starling (Manchester University), and "The good examples from Australia" by Anne McKenzie (University of Western Australia).

A panel debate including Bettina Husebø, Rune Samdal, Roger Strand and Tor Jacob Moe elucidating ethical, personal, and psychological implications of exposing user representatives to the high expectations from research environments, provided a new dimension to the topic.

Group sessions included both pre-arranged case discussions as well as each research school participants bringing forward their own projects for scrutiny, discussion, and advice from user representatives. Finally – the researchers presented the highlights from these group sessions in plenary sessions, also revealing custom-made take-home messages from the user representatives.

Of the 55 participants, 28 were user participants from a wide variety of user organizations. Among the 27 researcher participants, around half were PhD candidates and the rest were medical professionals. Nina Jebsen (CCBIO), Kjell-Morten Myhr (Neuro-SysMed) and Tone Skår (Neuro-SysMed/VIS) have the academic responsibility for CCBIONEUR910, and PhD candidates Hilde Norborg (Neuro-SysMed) and Pål Tore Bentsen (CCBIO) are the course coordinators.

CCBIONEUR911 – Clinical Trials in Cancer Research
CCBIONEUR911 is a new 2 ECTS course on clinical trials. The course is based on a course qualifying for a Good Clinical Practice (GCP) certificate held in 2019, and at that time organized by Line Bjørge and Hani Gabra. In 2021 it was expanded as a collaborative effort with Neuro-SysMed and run as an ECTS giving course in addition to qualifying for the GCP certificate.

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 modules are based on the ICH GCP, and cover topics from design planning to execution, such as general principles of clinical trials, ethics and the patient perspectives, GCP overview, operations and practicalities, formalities and regulations, translational research protocols, making clinical trials part of normal clinical operations, success factors and clinical trials in the future. Examples from cancer research and neurological research are embedded in the sessions.

The course took place September 29 – October 1, 2021, in a hybrid on-site/online format. Of the 60 participants, 17 opted for online attendance and about half the lectures were held digitally. Participants were a blend of MD/PhD-fellows, postdocs, researchers as well as students from the Medical Student Research Program. In addition to lectures, the participants were engaged in group work with presentations, where they discussed interesting ethical issues in clinical studies within the fields of cancer research and neurology, emphasizing autonomy, beneficence, and justice.

Line Bjørge (CCBIO) and Øivind Grytten Torkildsen (Neuro-SysMed) have the academical responsibility for CCBIONEUR911, and Benedicte Sjo Tislevoll (CCBIO) and Hilde Norborg (Neuro-SysMed) are the course coordinators.

CCBIONEUR912 – Health Innovation Course
CCBIONEUR912 is a brand new 4 ECTS course and the first PhD course at the UiB with a focus on health innovation. As such, it is an invaluable opportunity, especially for early career

medical researchers, giving insights on how to bring research to society and perspectives on alternative entrepreneurial career paths. The course also contains inspiring lectures by people who have walked this path before them, to great effect and success. The overall aim is to encourage and enable PhD students and young researchers to identify and evaluate their own research projects' innovation potential. The Health Innovation course consists of two modules and in total four seminar days of synchronous work in addition to three modules of asynchronous online work. Team-based discussions and assignments are part of the asynchronous online program.

CCBIONEUR912 is a collaboration between CCBIO and Neuro-SysMed and benefits greatly from affiliates of both centers with innovation experience. The course presents its participants with a wide variety of "problems" and "solutions" and routes to exploitation of research-driven innovations.

At the opening ceremony, CCBIO Centre Director Lars A. Akslen and Neuro-SysMed Director Kjell-Morten Myhr both emphasized the importance of innovation in research centers. Senior Adviser Yves Aubert from the UiB's Division of Research and Innovation discussed the UiB's societal mission and the government's main goal to strengthen competitiveness and innovation capability to meet major societal changes. Aubert also presented similarities and differences between research and innovation and explained how to build innovation into research projects and project proposals. The students were introduced to the available funding instruments for the various stages of development from Tine Torbjørnsen at the Norwegian Research Council. The students also had the unique opportunity to familiarize themselves with the perspective of early-stage venture capital funds from Farzad Abdi-Dezfuli, PhD and partner at Sarsia Management AS. Helge Ræder, Pro-Dean for Innovation at the Medical Faculty, talked about the innovation culture and mindset shift at the Medical Faculty and the incentives for PhD students and younger researchers to innovate. Senior Advisor for Innovation and Research at the Faculty of Medicine Andreas Westermoen introduced the students to the legal and practical framework for research-based innovation, including how to protect and exploit their intellectual property. Kine Gregersen, key account manager of the Health/Medical division of the tech transfer office VIS, introduced the students to the process from idea to exploitation in the pipeline of VIS, and highlighted the importance of user involvement as well as a thorough evaluation of user needs in the process, a topic discussed further by Innovation Manager at VIS, Tone Skår. Jim Lorens highlighted how the rich innovation culture at Stanford University was an essential inspiration for his own career path and encouraged him to think outside the box. Emmet McCormack shared his insight in to what it actually takes to make a successful company like Kinn Therapeutics in addition to running a research lab. Karl Henning Kalland presented his research and the exciting work of the company he founded, Alden Cancer Therapy II. Jonny Klemetsen, CEO of Youwell, gave an interesting presentation of his company and their tools for digital interventions and health services. Professor Ingvild Vistad from the Department of Clinical Science gave an inspirational talk on LETSGO - a multifunctional app for follow-up after cancer treatment, and the associated ongoing clinical trial.

The students also watched several video presentations of medical technology innovations, by Neuro-SysMed research partner Mandar Jog as well as innovation partner Yayoi Sakaki from Project Ipsilon. Professor Charalampos Tzoulis from Neuro-SysMed commented on the innovations from both a physician and researcher perspective and discussed them with the students.

An absolute highlight was the inspirational talk in the keynote lecture by Professor Robert Langer (see separate article in the Meetings section). Other highlights were the sessions with Ingunn Johanne Ness and Ole Dahlberg, made available to a wider audience as a Special Seminar on Creativity and Innovation Leadership (see separate article in the Meetings section). The Design Thinking workshop tailored especially to the PhD students, also scored very high on the student's evaluations. This engaging and intense 5-hour workshop was created and arranged by Federico Lozano, Susan Johnsen and Yves Aubert, and focused on how to achieve human-centered innovation and an open mindset that facilitates the generation, testing and exploitation of creative ideas and solutions. The students were also told to develop a "solution" to a selected problem and deliver their investor pitches to an expert panel consisting of Yves Aubert, Maija Slaidina and Andreas Vestermoen. As intended, this assignment brought the students slightly out of their comfort zone, enhancing their learning.

The course was held for the first time November 8-9 and December 2-3, 2021, with onsite participation by 18 students in the brand-new facilities of EITRI Medical Incubator. Several of the PhD students attending were from the CCBIO and Neuro-SysMed research environments, and quite a few from the Department of Clinical Odontology, constituting a good mix of researchers with different backgrounds, such as natural scientists and medical doctors, consultants in oncology and also students from the faculty's Medical Student Research Program, altogether contributing with a very broad range of projects.

Agnete Engelsen (CCBIO) and Magnus Alvestad (Neuro-SysMed) have the academic responsibility for CCBIONEUR912, and Ning Lu (CCBIO) and Hilde Norborg (Neuro-SysMed) are the course coordinators.

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 the 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, attending 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 exceed 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, inspiring, and challenging, 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 and 2021 but were postponed due to the pandemic. The program will be resumed when possible.

International Collaboration and Further Development of Courses

CCBIO has a 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 students and researchers and other interested staff to meet and interact with influential experts in the cancer research field.

As part of CCBIO's internationalization effort, a project under the RCN and HK-dir 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 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 and developing new curriculum to be used in the years to come.

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 been part of this activity. The students have reported great educational and scientific benefit from their Boston stay. The program will be resumed as soon as pandemic-related travel restrictions are lifted.

- A 4-day CCBIO-VBP Research Meeting was held at Iceland in 2019 and we aim to have a similar meeting in the fall of 2023. Such meetings allow faculty and students from CCBIO and VBP to meet and deepen their collaboration, educational as well as scientific, and discuss their projects and establish new collaborations.

- 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's application for renewed funding of it INTPART project received excellent reviews and a further three years of funding. The aim is 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 CCBIONEUR910-912 and its other activities together with its many excellent partners. Further courses will be established if needed. ••

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 research and stimulate discussions. In addition, each meeting includes a keynote lecture given by a more senior person, often someone from a different field of expertise. Students, PhD candidates, postdoctoral fellows, researchers, CCBIO affiliates, 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 different 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 four symposia, and write four reports summarizing four different presentations.

Due to the pandemic, all four symposia were held through digital platforms throughout 2021. The last symposium of the year was planned to be held as a physical meeting. However, the reintroduction of local pandemic measures required the organizers to relocate to a digital platform at very short notice. Although participants were not able to meet in person during 2021, the four digital Zoom meetings were well received, each with 20-30 participants and many fruitful discussions. Digital symposia also enabled CCBIO affiliates and collaborators outside of Bergen and Norway to attend, and the organizers appreciate that a broader audience has been attending the junior symposia this year.

Each JUSS included presentations from students, PhD candidates and postdoctoral fellows or other researchers at an early career stage. In addition, the symposia featured interesting keynote presentations from experienced researchers. The first keynote speaker in 2021 was Professor Hrvoje Miletic who gave an exciting lecture on therapy resistance in glioblastoma, providing inspiring insight into the world of translational research in brain cancer. The next keynote lecture was held by researcher Gro Vatne Røsland who gave an overview of what is known about the symbiotic relationship between humans and microbes. This is a field of research that has gained increasing interest lately as microbiota has been recognized to play important roles in various diseases, and the keynote lecture by Røsland was met by great enthusiasm. The symposia also featured keynotes from senior- and head engineers Hege Avsnes Dale and Hans Olav Rolfsnes from the core facility Molecular Imaging Center (MIC). They introduced the audience to a range of advanced microscopy techniques, covering imaging of cells, tissues, and small animals. In addition, they provided lots of good advice on acquiring imaging data as well as on how to analyze such data for scientific purposes, providing useful knowledge and inspiration for the participants.

The organizers were happy to see that both presenters and audience have adapted well to online participation, contributing with high-quality presentations, discussions, and enthusiasm, and 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 2022 to enjoy the discussions and possibilities for informal interaction and informal networking during breaks.

In 2021, the Junior Scientist Symposia were organized and chaired by Cornelia Schuster, Maria Lotsberg and Hanna Dillekås. ••

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
February 25, 2021
Digital event in Zoom

Symposium chairs:
Cornelia Schuster and Maria Lie Lotsberg

09:00-09:05 Organizers: Welcome

09:05-09:25 Lise Ingebriktsen: "Identification of an age-related breast cancer gene expression signature with strong prognostic value"

09:25-09:45 Katrin Kleinmanns: "CD24-targeted intraoperative fluorescence image-guided surgery leads to improved cytoreduction of ovarian cancer in a preclinical orthotopic surgical model"

09:45-10:00 Break

10:00-10:45 Keynote lecture by Hrvoje Miletic: "Glioblastoma treatment resistance – is there a way out?"

10:45-11:15 Break

11:15-11:35 Irmelin Wilhelmsen Nilsen: "Cancer, imaginaries and sensation journalism"

11:35-11:55 Hilde Lien: "Multiplex analyses of tumor heterogeneity in low-risk endometrial carcinomas"

11:55-12:00 Closing remarks

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
June 17, 2021
Digital event in Zoom

Symposium chairs:
Cornelia Schuster and Maria Lie Lotsberg

09:00-09:05 Organizers: Welcome

09:05-09:55 Keynote lecture by Gro Vatne Røsland: "Microbiota in health and diseases – a short overview"

09:55-10:15 Break

10:15-10:35 Cara Wogsland: "Advancing human cancer research with murine tumor models and mass cytometry"

10:35-11:05 Camilla Ekanger: "Human organotypic airway and lung organoids for the study of SARS-CoV-2 infectivity and cytopathology"

11:05-11:25 Break

11:25-11:45 Stephanie Gisela Schwab: "Tracking of systemic glioblastoma stem cells *in vivo*"

11:45-12:05 Shayla Sharmine: "Liquid biopsy in follow-up of metastatic melanoma treatment"

12:05-12:15 Closing remarks

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
September 16, 2021
Digital event in Zoom

Symposium chairs:
Cornelia Schuster and Maria Lie Lotsberg

09:00-09:15 Organizers: Welcome

09:15-10:00 Keynote lecture by Hege Avsnes Dale and Hans Olav Rolfsnes: "The Molecular Imaging Center – your local one-stop-shop for imaging cells, tissue and small animals"

10:00-10:15 Break

10:15-10:40 Kelly Marcela Velasco Pinto: "The SCHAD fatty acid oxidation enzyme in insulin secretion: Functional analyses of rare variants in human populations and a new murine model of congenital hyperinsulinism of infancy"

10:40-11:05 Stephanie Gisela Schwab: "Metastatic potential of systemic glioblastoma stem cell lines *in vivo*"

11:05-11:30 Break

11:30-11:55 Sushil Dhakal: "AXL inhibition enhances Type 1 interferon (IFN) response and potentiates chemo-immunotherapy"

11:55-12:20 Austin Rayford: "AXL targeting in the tumor immune microenvironment: translational insights from clinical trials"

12:20-12:30 Concluding remarks

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
November 11, 2021
Digital event in Zoom

Symposium chairs:
Maria Lie Lotsberg and Hanna Dillekås

09:15-09:20 Organizers: Welcome

09:20-09:45 Calum Leitch: "Drug development for acute myeloid leukaemia"

09:45-10:05 Break

10:05-10:30 Stein-Erik Gullaksen: "Single cell immune and signaling profiles of chronic myeloid leukemia: modulation of cell population and intracellular signaling early after start of therapy"

10:30-10:55 Amalie Fagerli Tegnander: "AGR2 in breast cancer – part of the estrogen receptor-related cancer biology?"

10:55-11:40 Break

11:40-12:05 Kala Chand Debnath: "Metabolic coupling between oral cancer cells and fibroblasts promotes a stem cell-like and migratory phenotype"

12:05-12:30 Elaheh Mahootchi: "GADL1 is a multi functional decarboxylase with tissue-specific roles in β-alanine and carnosine production"

12:30-12:40 Concluding remarks


Translation


Starting an
Independent lab

CCBIO
RESEARCH SCHOOL
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CCBIO MASTERCLASS PROGRAM

The aim of the CCBIO Masterclass training program is to prepare selected up-and-coming post-PhD researchers for a successful transition to their next career step, namely establishing independent research profiles, funding portfolios and their own research groups. Each masterclass class consist of up to 10 researchers who receive individual mentoring as well as a total of 6-7 plenary sessions.

Through the mentorship program, each candidate is assigned an experienced CCBIO mentor from outside of their own group. Together, they focus on guiding the mentee's career development, both in a broad sense and in setting up short- and long-term goals. Regular meetings allow for both planning and follow-up. Plenary sessions focus on a range of topics related to the following:

- **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**

Throughout the sessions, the candidates receive targeted input from CCBIO's PIs, network and administration, as well as from staff from the Medical Faculty, UiB's HR department, and the university library. Each Masterclass period is concluded with a two-day retreat together with CCBIO PIs, mapping out and deliberating upon each candidates' career plan. The Masterclass program is coordinated by CCBIO's Research Advisor Yamila Torres Cleuren.

In addition to Session 1 on application writing held in late 2020, CCBIO had a total of 4 Masterclass sessions in 2021. The sessions were highly interactive, with all participants taking an active role in the ensuing discussions, thereby gaining the full advantage of having such experienced speakers at their disposal. In Session 2, the focus was on how to conceptualize a research project and ensure its feasibility, and the participants benefitted from the accumulated experience of Neuro-SysMed Co-Director Charalampos Tzoulis and CCBIO PI Line Bjørge. Session 3 featured CCBIO's Director Lars A. Akslen talking about his experience forming his research team, and CCBIO Associate Investigator Daniela Costea about the tasks of a group leader. With vaccination rates up and COVID cases down, Session 4 became the first in-person session, letting the participants themselves present and discuss their individual plans in plenum, with a focus on establishing strong networks and collaborations, and how to overcome their career obstacles. Session 5 was coordinated by Research Advisor Amra Grudic-Feta (while Yamila was on maternity leave) and started with staff from Smart Start UiB holding a session on leadership in the broad sense, followed by two sessions held by CCBIO's administration leader Geir Olav Løken focused on how to navigate "the system" within the institution and on project management. Due to the deteriorating COVID situation, Session 6 on Science Communication and the final two-day retreat to summarize the experiences and hammer out concrete career plans for each candidate, were re-scheduled for the spring term of 2022.

The CCBIO Masterclass Program has received very positive feedback from the participants, their mentors, and the research groups. The participants even stated that it would be worth the while for institutions to have similar coaching arrangements tailored for each career stage, from the early PhD-level and onwards. Being integrated in rather small close-knit groups, it has also led to establishment of new scientific collaborations between the participants. The mentors felt that they had benefitted greatly from mentoring young researchers from outside of their own groups and have stated their intent to continue the arrangement with their mentees also after the current Masterclass period expires.

The perhaps clearest and most easily quantifiable outcome of the Masterclass program and CCBIO's support for younger researchers thus far, is that two of the participants received their first research funding as PIs at UiB. Heidrun Vethe, as co-PI, was awarded 8 mill NOK from The Norwegian Cancer Society, and Carina Strell received a 20 mill NOK starting grant from the Trond Mohn Foundation. This reflects the high impact that such targeted programs and in-depth application writing support can have on kickstarting the careers of early-stage researchers.

CCBIO aims to continue its Masterclass program with a new class starting in the fall term of 2022. The continued program will benefit from the experiences from the first class, from the feedback from participants, speakers, and mentors, and offer targeted support to foster the careers of new candidates. By continuing to support early-stage researchers in this way, CCBIO hopes to jump-start the next stage of the participants' research career, and to make a lasting impact. ••

HARSH DONGRE has a PhD from the UiB focusing on the role of tumor stroma in progression of squamous cell carcinomas. Since 2020, he is a postdoc in the Costea and Bjørge groups, working on differential mechanisms of tumor-stroma interactions in human papilloma virus (HPV) positive and negative carcinomas. Dongre is now working to understand cancer associated fibroblast (CAF) heterogeneity and how this drives cancer progression using imaging mass cytometry and single cell sequencing. The long-term focus is to understand the role of the tumor microenvironment in progression of various tumors and to develop novel nanodiamond based theranostic strategies in which both transformed cells and activated stroma can be co-targeted. Dongre aims to establish his own research group, combining multidisciplinary skill sets to focus on nanotechnology based theranostic strategies.

AGNETE ENGELSEN has a PhD in biomedicine from the UiB on intra-tumoral heterogeneity in glioblastoma. Since 2013, she has been affiliated with CCBIO, first as a postdoc in the Lorens' group, and later as a visiting researcher at the Gustave Roussy Cancer Center (Paris). Engelsen is dedicated to exploring how phenotypic plasticity interferes with therapeutic efficacy and immune cell-mediated killing. Through interdisciplinary collaboration, Engelsen has established non-small cell lung cancer patient-derived organoid and explant models recapitulating the complex tumor-immune microenvironment. With these models, her current project aims to elucidate the effect of phenotypic plasticity on the spatial organization of the tumor immune microenvironment and explore how targeting phenotypic plasticity may synergize with immune checkpoint inhibition therapy, which serves to release the brakes that cancer cells can put on the immune system.

DIMITRIOS KLEFTOGIANNIS has a PhD in computer science and bioinformatics from Kalnis' group at KAUST, focusing on computational identification of enhancers and promoters using big genomic and epigenomic datasets. Currently he is a postdoc working with the Jonassen and Akslen groups at the UiB and CCBIO. Kleftogiannis is developing computational methods for single-cell data analysis coupled with machine learning modelling approaches to decipher complex cancer progression mechanisms. He is involved in national and international projects aiming at supporting his scientific independence as a junior group leader in the field of computational cancer research.

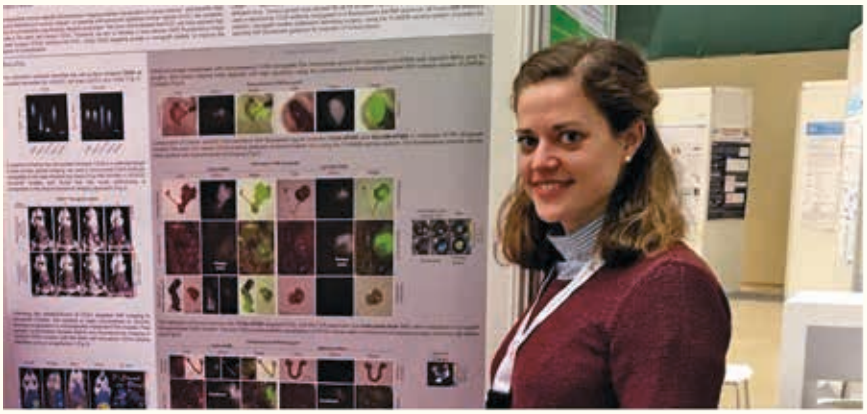
KATRIN KLEINMANNS has a PhD from the UiB and is currently a postdoc in the McCormack and Bjørge groups. Her research focuses on the development of immunocompetent patient-derived xenograft (PDX) models of ovarian carcinomas to improve therapeutic interventions through novel immune therapies and targeted fluorescence image-guided surgery. The focus is on genomic and phenotypic characterization of PDX models including the verification of genomic fidelity to the paired primary tumors as well as phenotypic mapping of the tumor microenvironment. Kleinmanns aims to provide good and reliable preclinical animal models combining the interactions of the human immune system and genomic evolution of tumor cells. She prepares to go abroad, focusing on mRNA-based immunotherapy and novel CAR T cell designs. Her goal is to establish her own group within the field of Cancer Immunotherapy.

MARI KYLLESØ HALLE has a PhD from the UiB on molecular alterations suggesting new treatment strategies in uterine carcinomas. She is currently a researcher in the Krakstad group, working on gynecological cancer. Her main focus is to characterize targetable molecular alterations driving aggressive uterine cancer. Currently, she is comparing and combining radiomic features from whole tumor segmented magnetic resonance imaging (MRI) scans with genomic profiles. This radiogenomic approach might detect novel prognosticators for disease outcome and new treatment strategies in cervical cancer. Halle is currently applying for available grants to continue her research on uterine cancers, with the goal of establishing her own research team focusing on translational cervical cancer research.

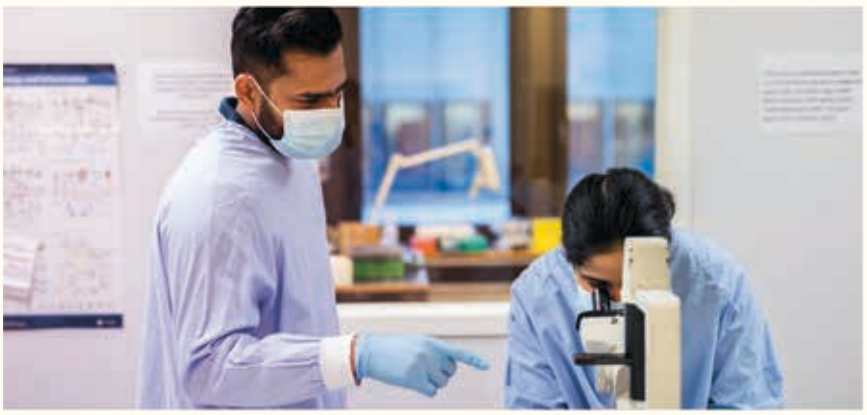
CARINA STRELL has a PhD from the University of Witten-Herdecke in Germany on tumor-immune cell interactions. She thereafter did a postdoc with Arne Östman at the Karolinska Institute, where she studied the impact of the tumor microenvironment on progression and therapy resistance of breast ductal carcinoma *in situ* (DCIS). Strell is currently an associate professor at Uppsala University within the research group of Patrick Micke and member of the CCBIO international faculty, and she will join CCBIO in June 2022 as an associate PI with a start-up grant from the Trond Mohn Foundation (TMS). Her ongoing research aims to decipher the molecular regulators of early breast cancer evolution using a spectrum of spatial techniques for tissue analysis and patient-derived organoid models. Strell hopes to uncover novel biomarkers to improve treatment strategies for women with early breast cancer and to identify therapeutical targets to overcome therapy resistance. She aims to establish an independent team on early breast cancer evolution at CCBIO.

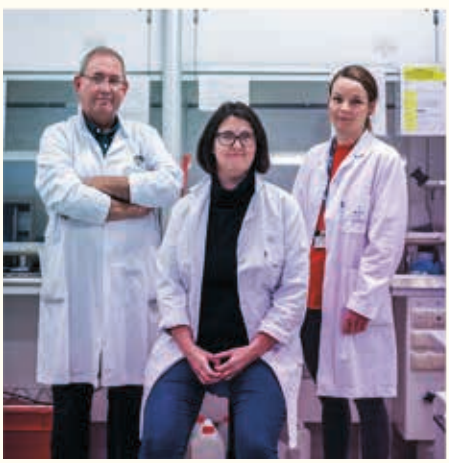
LIV CECILIE VESTRHEIM THOMSEN has a PhD from the UiB focusing on the genetic background of complex diseases. She is currently a researcher in the Bjørge group and also associated with the Gjertsen group. Her main focus is on mass cytometry (CyTOF) analyses, developing antibody panels for immune cells 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, hoping to detect molecular signatures that can reflect the underlying biology of these tumors as well as treatment responses. Her long-term professional aim is to establish independency and her own research group.

HEIDRUN VETHE has a PhD from the UiB on stem cell research and diabetes. She is currently a postdoc in the Akslen group, focusing on nerve involvement in breast cancer progression. The project combines imaging mass cytometry analysis of patient material and cellular models to investigate the role that nerves play in driving aggressive tumor traits in primary and metastatic breast cancer, and Vethe has as co-PI recently been awarded 8 mill NOK from the Norwegian Cancer Society for this project. After the postdoc period, Vethe aims to secure further funding for her research in order to achieve scientific independence as a young investigator in the field of breast cancer neuroscience.



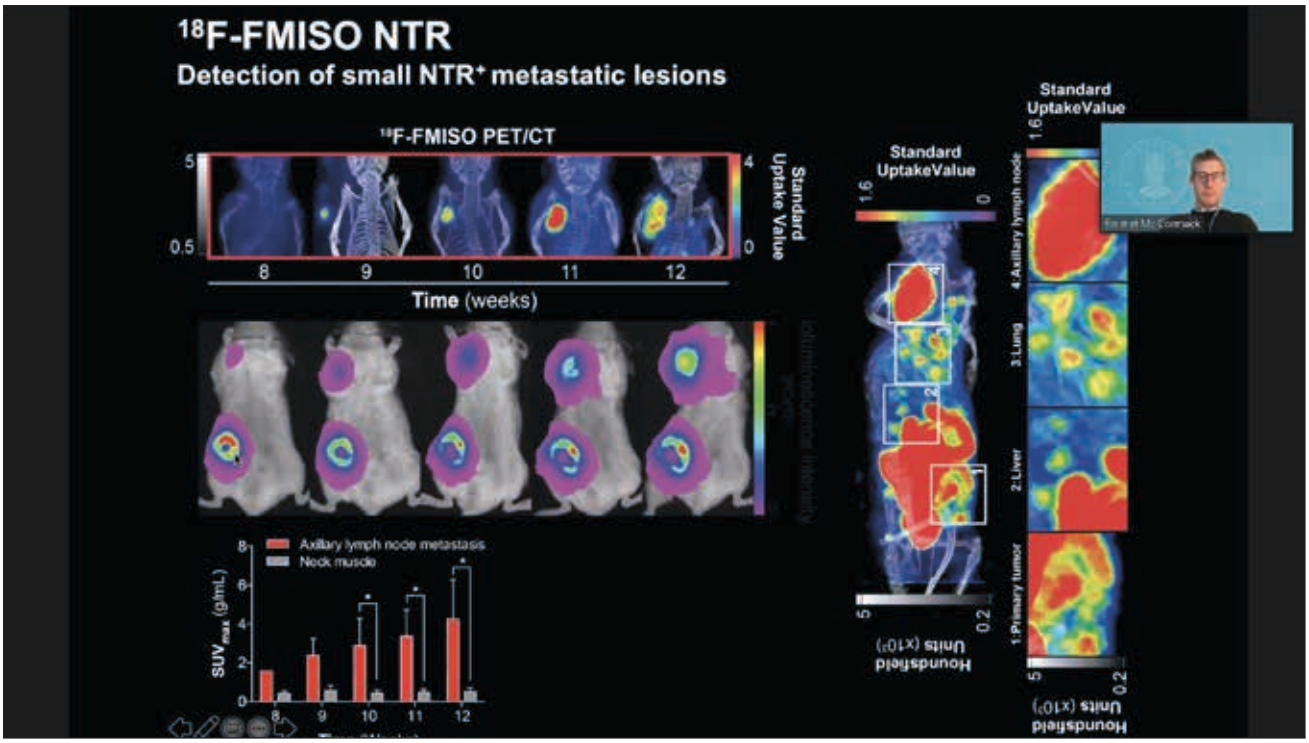






Cancer Biomarkers

CCBIO RESEARCH SEMINARS



CCBIO's monthly research seminars gather a wide range of researchers and others with a common interest in cancer biomarkers for updates on cutting edge research. The speakers are mainly international, and all are of a high international standard. Being open to all, the seminars are well visited, also by staff outside of CCBIO.

The seminar series' main aim is to convey relevant biomarker research to CCBIO staff and 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 researchers, in particular the younger ones, get the opportunity to discuss projects and collaboration with high level scientists. Normally, each seminar is followed by an informal pizza get-together, making the CCBIO Seminars an arena for informal crosstalk that both strengthens cohesion and often leads to fruitful scientific collaborations.

Since the spring of 2020 and throughout 2021, all CCBIO seminars were held digitally due to the pandemic. As gathering CCBIO would mean mustering staff from a wide array of hospital departments, we opted for digital seminars also during the periods with a low degree of contagion. In retrospect, this rather conservative approach turned out to be well founded. A CCBIO spreader event might have had serious consequences for the region's largest hospital and its patients. The surge in infections in late autumn 2021, a renewed semi-lockdown, and instances of COVID-infections at the hospital proved this policy right.

CCBIO 's digital research seminars turned out a success, with good attendance and increased participation from abroad, also from overseas. 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 is coordinated by Donald Gullberg, and forms part of the PhD-level course CCBIO902. CCBIO Seminars are also a part of the master-level course BMED380, for which Beate Stern and Gro Vatne Røsland are the course coordinators. Since the start in 2013, the collaboration with the BMED380 group has been a success, benefiting both CCBIO and the Department of Biomedicine. 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 the digital lectures, also from abroad. ••

CCBIO Research Seminars in 2021

During 2021, a range of cutting-edge topics were covered, most of them by international speakers. For the December meeting, a seminar was given by professor Eystein Jansen from the world-famous Bjerknes Centre for Climate Research in Bergen. Although a different topic, this talk was most stimulating with transferrable knowledge on strategy and how-to-do-it.

JANUARY 28, 2021
Arne Östman, Department of Oncology-Pathology, Karolinska Institute (KI), Sweden: Cancer-associated fibroblasts; novel subsets associated with tumor biology features, outcome and response to treatment. Chair: Lars A. Akslen

FEBRUARY 25, 2021
Mark LaBarge, Department of Population Sciences, Beckman Research Institute at City of Hope, Duarte, CA, USA: Epigenetic priming in mammary epithelia underlies susceptibility to age-related cancers: causes, consequences, and countermeasures. Chair: Agnete Engelsen

MARCH 25, 2021
Randolph Watnick, Vascular Biology Program, Boston Children's Hospital, and Department of Surgery, Harvard Medical School, Boston, MA, USA: Identification of a novel paracrine acting stimulator of tumor growth and progression via modulation of Tsp-1 in the tumor microenvironment. Chair: Lars A. Akslen

APRIL 29, 2021
Ian Mills, Centre for Cancer Research and Cell Biology, Queen's University Belfast, Northern Ireland, and Nuffield Department of Surgical Sciences, University of Oxford, UK: Non-oncogene addiction and the stress phenotype of prostate cancer cells. Chair: Karl-Henning Kalland

MAY 27, 2021
Ellen Puré, Department of Biomedical Sciences, University of Pennsylvania, Philadelphia, PA, USA: Flanking solid tumors via immune-mediated disruption of desmoplastic stroma. Chair: Donald Gullberg

JUNE 10, 2021
Andrew Leask, School of Dentistry, University of Saskatchewan, Saskatoon, SK, Canada: Micro-environmental control of fibrosis: a central role for the CCN family of matricellular proteins. Chair: Donald Gullberg

AUGUST 26, 2021
Hege F. Berg, the Bergen Gynecologic Cancer Research Group, CCBIO, University of Bergen: Endometrial cancer model systems to improve treatment. Chair: Harsh Dongre

SEPTEMBER 30, 2021
Emmet McCormack, Department of Clinical Science / CCBIO, University of Bergen: Imaging preclinical tumor models: improving translational power. Chair: Bjørn Tore Gjertsen

OCTOBER 28, 2021
Sebastian Marwitz, Lung Research Center in Borstel, Germany: A pathway and spatial biology approach to NSCLC. Chair: Donald Gullberg

NOVEMBER 25, 2021
Emily Arner, Brekken lab at UT Southwestern Medical Center, Texas, and the Rathmell lab at Vanderbilt University Medical Center, Nashville, USA: AXL-TBK1 driven nuclear AKT3 stabilizes snail/slug to promote EMT. Chair: Jim Lorens

DECEMBER 16, 2021
Eystein Jansen, Bjerknes Centre for Climate Research, University of Bergen: Climate Research in Bergen - Strategic choices and challenges that paved the way. Chair: Lars A. Akslen

CCBIO SPECIAL SEMINARS AND MEETINGS

When CCBIO members have something particularly interesting to convey or they have senior researchers visiting or taking part in courses outside of the monthly 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 and to attend meetings going deep into especially interesting topics.

The first half of 2021 was strongly influenced by the continued social distancing measures, whereas the activity picked up somewhat in the autumn, allowing for gatherings of several hundred people, before the rising COVID case load again prompted a renewed semi-lockdown. We hope for a considerable increase in such seminars and meetings throughout 2022.

October 20, 2021 // Celebration seminar for Cancer Research Prize to Bjørn Tore Gjertsen. CCBIO Special Seminar to celebrate the awarding of King Olav V's Prize for Cancer Research 2021 to CCBIO PI and Co-Director Bjørn Tore Gjertsen. Prior to the seminar on October 20, an award ceremony took place in Oslo on October 18, 13.00-14.00, when H. M. King Harald presented the prize to Professor Gjertsen.

The event was splendidly opened by a quintet from Eikanger-Bjørsvik Musikklag, one of the best brass bands in Europe, and with which Gjertsen has a personal relationship as he played the cornet and flugelhorn there for many years. CCBIO's Director Lars A. Akslen gave a short introduction, describing

Gjertsen as a true "translationist" within Norwegian cancer research, with a strong focus on basic studies combined with exceptional clinical engagement and commitment to his patients, colleagues, and students. Several invited guests were present, among them all six previous winners of this award at the Medical Faculty, University of Bergen. Congratulatory speeches were also given by Per Bakke, dean of the Faculty of Medicine, UiB, and Eivind Hansen, CEO of Helse Bergen, as well as Astrid Olsnes Kittang, head of the Hematology section, Haukeland University Hospital (HUS), Eystein Husebye from the management of the Department of Clinical Science, UiB, and Steinar Skrede, assistant director at the Medical Clinic, HUS. The scientific part of the program consisted of talks by collaborators from throughout Gjertsen's career: Professor emeritus Stein Ove Døskeland, Professors Emmet McCormack, Line Bjørge, Stian Knappskog and Oddbjørn Straume, and Gro Gausdal, Director of Research at BerGenBio ASA.

The Bergen research community's recipients of the King Olav V's Prize for Cancer Research. From the left: Stein Ove Døskeland (1995), Rolf Bjerkvig (2015), Per Eystein Lønning (1999), Bjørn Tore Gjertsen (2021), Lars A. Akslen (2009), Olav Dahl (2013) and Per Magne Ueland (1992)

Before Akslen provided the concluding remarks, Gjertsen gave the talk "Novel diagnostics and adaptive cancer therapy", where he presented an overview of targeted and individualized cancer therapy as well as functional drug response testing and personalized medicine in leukemia, the field for which he received the award. He also looked towards the horizon with an inspiring take on the future of precision medicine.

Following the autumn lull in COVID cases, the Celebration Seminar was a joyous opportunity to finally be able to gather at Campus Haukeland for a large event with around 250 on-site attendants in Store Auditorium. When the formal program was completed, the discussions and celebration continued for two hours with tapas and cake.

November 11, 2021 // Falch Lecture 2021: Professor Robert S. Langer. Professor Robert S. Langer, Massachusetts Institute of Technology, "The Edison of Medicine", presented the Falch Lecture entitled "Creating and implementing breakthrough technologies in biotechnology and nanotechnology". Dr. Langer was nominated to the Falch Lecture by CCBIO Director Lars A. Akslen and the Neuro-SysMed Director Kjell-Morten Myhr, who also held a digital pre-meeting with Langer before the lecture. Helge Ræder, Vice Dean for Innovation at the Medical Faculty, hosted the lecture.

Dr. Langer was able to connect superbly with his audience of more than 200, despite being on a live streaming rather than in-person, vividly describing his trials and tribulations as well as his journey to academic recognition. In sum, his lecture conveyed the impression of a "scientific giant" whose accomplishments can only be described in historic terms. The attendants also met the human whose dedication and sheer perseverance overcame scientific, institutional and entrepreneurial barriers, especially during the early years. At the same time, Dr. Langer takes much pride in the successes

of his former students and fellows, while attributing his own breakthrough also to his mentor, the late Dr. Judah Folkman, who believed in him, and inspired and supported him during his formative post-doctoral years.

In terms of more recent achievements, the fact that it took Moderna – a company co-founded by Dr. Langer – only 64 days from receiving the genetic code of SARS-CoV-2 from

Chinese scientists, to administering Moderna's COVID-19 vaccine for the first time to humans, is truly mind-boggling. At the same time, Langer showed that this is the result of a combination of visionary science and entrepreneurial preparedness and maturity.

In the Q&A session that followed the Falch Lecture, Langer shared important insights, e.g. that great innovations are typically the result of bold, curiosity-driven research; that it takes well-funded, expert institutional support to transition research results to new treatments that save lives; that perseverance is key, especially during difficult times; and that both international collaboration and a healthy portion of competition are important factors for scientific breakthrough and entrepreneurial success.

The lecture was followed by a social event at Eitri Medical Incubator where the participants enjoyed a generous amount of finger food in each other's company.

Watch a video recording of Dr. Langer's lecture

December 2, 2021 // Special Seminar on Creativity and Innovation Leadership. As an integral part of the course CCBIONEUR912 Health innovation, CCBIO and NeuroSysMed invited a broader audience to an open Special Seminar on Creativity and Innovation Leadership with invited speakers Ole Dahlberg and Ingunn Johanne Ness. The Special Seminar focused on topics like: How to foster creativity in your organization and create a sustainable innovation culture. How can you develop yourself into becoming an innovative leader and encourage your team to be courageous in their efforts and ideas? What personal qualifications and "markers" are international life science industry leaders looking for when building well-functioning teams and recruiting trainees and the leaders of tomorrow? The event was open to all and the autumn lull in COVID cases allowed it to be well attended.

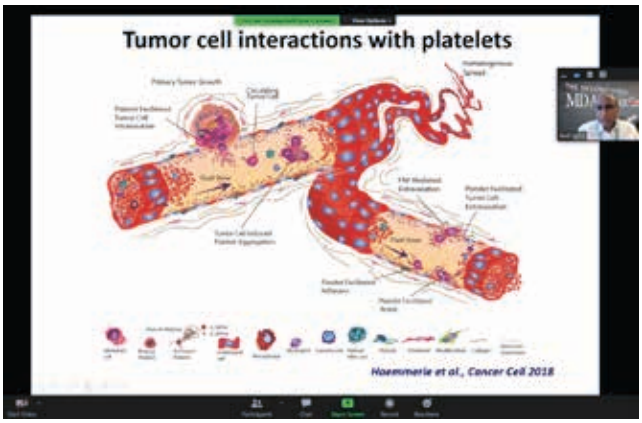
Senior researcher Ingunn Johanne Ness from the Centre for the Science of Learning and Technology at the Faculty of Psychology, UiB, introduced the students to the extensive research she has conducted on the topic of collaborative creativity in strategy and innovation contexts since 2009, and she talked about how to overcome barriers to innovation and increase the level of trust and engagement to create and maintain well-functioning creative teams.

Next, the participants had the opportunity to learn from the personal journey and reflection of Ole Dahlberg, a sought-after international life science leader who was brought over from his leadership role in a Norwegian Biotech Company to become VP and GM at Thermo Fisher Scientific in California. To prepare young researchers for a constantly changing complex world, Dahlberg highlighted five key skills that should be an essential part of their education: critical thinking, collaboration, communication, creativity - and ethics. Dahlberg further highlighted passion for what you are doing and the ability to act decisively as two of the most important hallmarks he was looking for when recruiting. Dahlberg, who is recognized for his inclusive and empowering leadership style, further emphasized the ability to handle complexity and the ability to collaborate as key capacities of aspiring leaders.

Following the talks, the participants engaged in lively discussions with the invited speakers, on topics related to career development, how to build trust in interdisciplinary teams and academia–industry collaborations, and how to empower people and act and implement more efficiently. ••

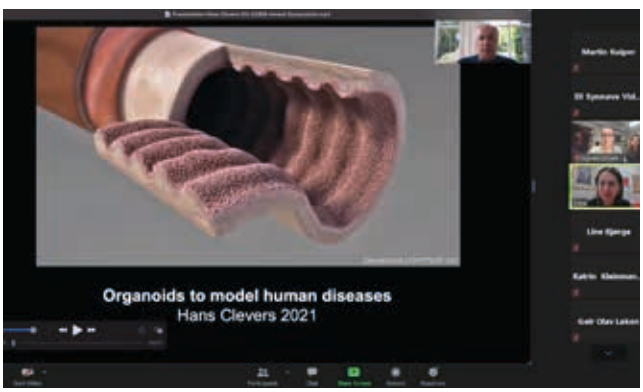
9TH CCBIO ANNUAL SYMPOSIUM 2021

Each year in May, CCBIO normally arranges its annual symposium at Solstrand Hotel outside of Bergen with more than 200 participants from Norway and a wide range of international institutions. The 2020 symposium sadly had to be cancelled due to the pandemic. In May 2021, however, the research community's skills with online solutions were on a wholly different level, and the 9th CCBIO Symposium took place online. Hence, May 19 and 20, more than 330 participants from several corners of the world gathered on Zoom, being able to hop in and out of the lectures and presentations at their leisure.



The program started 11.00 AM each day to accommodate international colleagues located in various time zones, and was broadly composed, covering various fields and perspectives within cancer research. One of the highlights this year was Bernd Bodenmiller from the University of Zürich. Bodenmiller is a pioneer in advanced tissue analysis through imaging mass cytometry. This new technology, also used by CCBIO since early 2019, allows for deeper and more complex investigations of intact tumor tissues. This provides more credible outputs and perspectives for personalized medicine, helping to find the right drug for the individual person. Other highlights were Hans Clevers from the University of Utrecht with an intriguing talk on organoids, Klaus Pantel with great humor and a talk on liquid biopsy, and Anil Sood who discussed the rapidly expanding treatment options for ovarian cancer, particularly focusing on angiogenesis as a target. The speaker list also included highly interesting talks by Ulf Landegren on molecular tools for biomarker analysis in immune oncology, Lewis Au on determinants of anti-PD1 response and resistance in renal cell carcinoma, Morag Park on tumor zonation and immune microenvironments in triple negative breast cancer, Ezra Cohen on neoantigen identification and use as biomarkers, and Genevieve Boland on multimodality approach to predicting and monitoring immunotherapy response and resistance, with interesting patient cases, emphasizing "the power of one" – studying one patient in depth. The participants also enjoyed Amir Aref's story on utilizing technology developed during his work at MIT, via the Dana Farber institute, to the establishment of the first company in the world on 3D culture of cancer cells, allowing for *ex vivo* tumor characterization. The program was also enriched by a talk from Jeffrey Pollard on monocyte regulation in homeostasis and malignancy, from Kara Davis on understanding leukemia heterogeneity using single-cell studies for clinical translation, Hani Gabra on regulation of receptor tyrosine kinases by OPCML – biology and potential therapies, and CCBIO PI Dana Costea, who walked the audience through 3D organotypic models of human squamous cell carcinoma.

As an alternative to the usual poster presentations by younger researchers, the program included 3-minute "speed presentations", a rather new pitch-style format where young researchers present their projects with a single slide. Over the two days, 32 young researchers presented their research, and each day the audience and a scientific committee decided on an audience award and chairs' award respectively. The audience was highly impressed with the young researchers' display of quality, innovation and entrepreneurship. The audience awards went to Luka Tandaric and Katrin Kleinmanns, and the committee awards went to Marta Espevold Hjelmeland and Karen Gissum.



Although this year's symposium was different and we sorely missed the informal on-site interactions and networking, it still provided lively discussions and CCBIO was able to attract a range of international top-notch speakers. It is however our most sincere hope that from 2022 and onwards, we will again be able to convene in-person at Solstrand with live streaming as a complementary format.

The next CCBIO Annual Symposium will take place May 10-11, 2022. ••

Centre for Cancer Biomarkers

9th CCBIO Symposium 2021

Virtual event in Zoom, May 19-20, 2021

SCIENTIFIC PROGRAM

Day 1: Wednesday May 19, 2021

10:45-11:00 Welcome and Opening;
Lars A. Akslen (Director of CCBIO)

Chairs: Karl-Henning Kalland and Oddbjørn Straume

11:00-11:45 Klaus Pantel: Liquid Biopsy: From discovery to clinical implementation

11:45-12:15 Ulf Landegren: Molecular tools for biomarker analysis in immune oncology

12:15-12:45 Lewis Au: Determinants of anti-PD1 response and resistance in renal cell carcinoma

12:45-13:00 Questions and Discussion

13:00-14:00 **Break**

Chairs: Camilla Krakstad and Liv Cecilie Vestrheim Thomsen

14:00-15:00 Speed presentations by young investigators (replacing posters)

15:00-16:00 **Break**

Chairs: Jim Lorens and Rolf Brekken

16:00-16:45 Bernd Bodenmiller: Highly multiplexed imaging of tissues with subcellular resolution by imaging mass cytometry

16:45-17:15 Morag Park: Tumor zonation and immune microenvironments in triple negative breast cancer

17:15-17:45 Ezra Cohen: Neoantigen identification and use as biomarkers

17:45-18:15 Genevieve Boland: Multi-modality approach to predicting and monitoring immunotherapy response and resistance

18:15-18:30 Questions and Discussion

Day 2: Thursday May 20, 2021

Chairs: Daniela Costea and Agnete Engelsen

11:00-11:50 Hans Clevers: Organoids to model human diseases

11:50-12:10 Daniela Costea: 3D organotypic models of human squamous cell carcinoma

12:10-12:40 Amir Aref: Patient derived organoids in cancer research

12:40-13:00 Questions and Discussion

13:00-14:00 **Break**

Chairs: Elisabeth Wik and Cornelia Schuster

14:00-15:00 Speed presentations by young investigators (replacing posters)

15:00-16:00 Break

Chairs: Line Bjørge and Bjørn Tore Gjertsen

16:00-16:30 Anil Sood: Ovarian cancer – understanding the mechanisms of adaptive resistance to anti-angiogenesis drugs

16:30-17:00 Jeffrey Pollard: Monocyte regulation in homeostasis and malignancy

17:00-17:30 Kara Davis: Understanding childhood leukemia through the lens of normal development: Single-cell studies for clinical translation

17:30-18:00 Hani Gabra: Regulation of receptor tyrosine kinases by OPCML – biology and potential therapies

18:00-18:15 Questions and Discussion

18:15-18:30 Bjørn Tore Gjertsen (Co-Director of CCBIO): Closing remarks

OTHER MEETINGS

While CCBIO is very satisfied with its annual symposium and seminar structure, our research groups also organize and contribute towards a range of other meetings and activities on their own initiative. As the pandemic subsides, we feel confident that this important part of our group´s activities will rebound to its previous level.

The Scandinavian Seminar on Translational Pathology (SCANPATH). The Scandinavian Seminar on Translational Pathology (SCANPATH) is a CCBIO-initiated annual network meeting for Scandinavian tumor pathologists and pre-clinical scientists with an interest in the prospects of next generation tissue profiling and research. SCANPATH aims is to stimulate tissue-based studies of tumor mechanisms and biomarker mapping. With the exemption of the pandemic related cancellation in 2020, this meeting has been an annual success since 2016 and is now a well-established Scandinavian forum. Since the first meeting in Bergen (2016), further meetings were held in Sigtuna, Sweden (2017), Gustavelund, Tuusula, Finland (2018), and Solstrand, Bergen (2019). This year's SCANPATH was held in Tylösand, Sweden, November 19-20, during the autumn lull in COVID cases, and was organized by Karin Jirström and her group from the University of Lund. The attendees were delighted to finally be able to meet in-person again.

Karin Jirström had composed a scientific program filled with inspirational and educational presentations by renowned researchers based in Norway, Sweden and Finland. Among others, Göran Jönsson explored the molecular landscape of immune checkpoints blockade resistance; Teijo Pellinen demonstrated intriguing methods for characterizing the cancer microenvironment by multiplex immunofluorescence; Arne Östman presented a novel fibroblast population associated with prognosis and treatment options; David Gisselsson Nord captivated the audience with a story about collateral clonal replacement in pediatric cancer; and Cecilia Lindskog provided an update to the Human Protein Atlas and continued efforts to characterize the human proteome. Carina Strell, a CCBIO international faculty member from the University of Uppsala, talked about epithelial-stromal interactions in breast cancer.

The participants from CCBIO actually constituted the largest single delegation at the meeting, and several had the opportunity to present their work, projects and future plans. Among them were the young CCBIO researchers Ole Bjørnstad, Kenneth Finne, Lise Ingebriktsen, Silje Kjølle, and Heidrun Vethe with oral presentations.

Despite adhering to the current COVID guidelines, there was still ample opportunity for informal interaction among the participants during dinner or in the spa at the hotel or relaxing in front of the beautiful windy beach that welcomed the participants in Tylösand.

SCANPATH 2021 was a very stimulating meeting with an opportunity to strengthen the already close ties between Scandinavian pathologists and basic scientists, as well as finally meeting friends and collaborators face to face again.

SCANPATH 2022 will be held at Solstrand close to Bergen November 14-15. ••

Centre for Cancer Biomarkers

5th SCANPATH

Scandinavian Pathology by the Sea – 2021

SCIENTIFIC PROGRAM

Day 1:	**Friday November 19, 2021**
09:00-09:25	**Registration and coffee**
09:25-09:30	Karin Jirström: Welcome
09:30-10:15	Göran Jönsson: Exploring the molecular landscape of immune checkpoint blockade resistance
10:15-10:45	Martina Bosic: Novel potential NK-cell markers in NSCLC
10:45-11:00	**Coffee break**
11:00-11:30	Teijo Pellinen: Multiplexed imaging of the tumor microenvironment
11:30-11:50	Arne Östman: Novel fibroblasts subsets associated with prognosis and treatment response
11:50-12:10	Feria Hikmet: Cancer-Testis Antigen and Immune Profiling in Non-Small Cell Lung Cancer by Transcriptomics and Antibody-Based Proteomics
12:15-13:15	**Lunch**
13:15-14:00	David Gisselsson Nord: Collateral clonal replacement - a mechanism for treatment resistance in childhood cancer
14:00-14:30	Alexandra Petersson: Genetic topography and immunogenicity in pancreatic cancer
14:30-14:40	**Coffee break**
14:40-15:00	Martina Bosic: Transcriptomic and proteomic heterogeneity of skin cells
15:00-15:20	Kenneth Finne: A stromal-based proteome signature provides independent stratification of luminal A breast cancer
15:20-15:40	Heidrun Vethe: Nerve involvement in breast cancer
15:40-15:55	**Coffee break**
15:55-16:40	Carina Strell: Progression and therapy-resistance of DCIS –impact of tumor-stroma interactions
16:40-17:00	Viktoria Thurfjell: Tracking ROS-1-fusion in NSCLC
17:00-19:00	**Spa**
19:00	**Dinner**
Day 2:	**Saturday November 20, 2021**
09:00-09:45	Cecilia Lindskog: The Human Protein Atlas – single cell omics for spatial mapping of the human proteome
09:45-10:05	Lise Ingebriktsen: Exploring the biology in young breast cancer
10:05-10:30	**Coffee break and check out**
10:30-10:50	Silje Kjølle: Luminal-like and basal-like breast cancer cell secretomes produce distinct CAF phenotypes
10:50-11:10	Yanhong Su: B cell landscape in undifferentiated pleomorphic sarcoma
11:10-11:30	Ole Bjørnstad: Neural progenitors and breast cancer spheroids
12:00	**Lunch and goodbye**

DISSERTATIONS

Our PhD candidates' doctoral defense is among the absolute highlights throughout the year. The award of a PhD is a celebration of the individual student's skills and development, as well as an expression of a long-term team effort, including supervisors, collaborators and support staff. We are also confident that 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 an important meeting place for junior scientists within cancer research 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 senior international researchers and establish new collaborations.

Throughout 2021, CCBIO had a total of 55 PhD candidates, of which 62% were female. 53% were of Norwegian origin. Among the remainder, Africa and Asia were particularly well represented with about a third.

We congratulate the following PhD candidates who successfully completed their degrees in 2021:

ANA BEATRIZ MATEUS D'AVÓ LUÍS

"Essays on Economic Incentives and Implications of Biomarker Tests." Supervisors: Professor Tommy Staahl Gabrielsen and Julie Riise, with contributions from Professors Lars A. Akslen, Roger Strand, John Cairns and PhD Kelly Seo. Defense date: February 12, 2021.

SHAMUNDEESWARI ANANDAN

"Rethinking High-Grade Serous Carcinoma: Development of new tools for deep tissue profiling." Supervisors: Professors Line Bjørge and Emmet McCormack and Researcher Liv Cecilie Vestrheim Thomsen. Defense date: September 3, 2021.

ELVIRA GARCÍA DE JALÓN VIÑEGRA

"Preclinical molecular imaging in oncology – From chemical synthesis to clinical translatable applications." Supervisors: Professors Emmet McCormack and Bengt Erik Haug. Defense date: June 25, 2021.

MOSES MUSIIME

"Novel tools and assays for the study of integrin $\alpha 11$ expression and function." Supervisors: Professors Donald Gullberg and Daniela Elena Costea. Defense date: September 24, 2021.

HILDE YTRE-HAUGE SMELAND

"Role of integrin $\alpha 11\beta 1$ in breast cancer." Supervisors: Professors Linda E. Birkhaug Stuhr, Lars A. Akslen, Donald Gullberg and Rolf K. Reed. Defense date: September 24, 2021.

DAVID ERIK FORSSE

"Novel preoperative biomarkers and evaluation of altered treatment strategies to improve outcome for endometrial cancer patients." Supervisors: Professors Camilla Krakstad and Jone Trovik. Defense date: October 1, 2021.

EIRIK JOAKIM TRANVÅG

"Precision and Uncertainty. Cancer biomarkers and new perspectives on fairness in priority setting decisions in personalized medicine." Supervisors: Professors Ole Frithjof Norheim, Roger Strand and Lars A. Akslen and Associate Professor Trygve Ottersen. Defense date: September 24, 2021.

ASTRID BØRRETZEN

"Epithelial-mesenchymal transition, angiogenesis, and molecular markers in aggressive prostate cancer." Supervisors: Professors Ole Johan Halvorsen, Lars A. Akslen and Christian Beisland. Defense date: October 22, 2021.

FACTS AND FIGURES 2021

CCBIO's scientific production reached an all-time high in 2021. For 2022, we expect somewhat lower numbers followed by a rise in 2023 as the last round of CoE financed PhDs, postdocs and researchers publish their results. External funding is generally good at 35% of total funds consumed in 2021. The numbers listed reflect the funds consumed each year, independent of grants received. Due to the pandemic, laboratories were shut down, equipment maintenance and repairs were delayed, there was a crunch on basic lab material and less in-person attendance to meetings. Also in 2021, this impacted our ability to use funds to the best possible effect. We expect our activities and use of funds to rebound fully in 2022-23. In terms of outreach, CCBIO is very active for a CoE within cancer research, with a substantial amount of communication output and mass media appearances.

PERFORMANCE INDICATORS	2013	2014	2015	2016	2017	2018	2019	2020	2021	TOTAL
PUBLICATIONS	76	71	77	85	94	81	79	79	126	768
COMPLETED PHDS	5	6	3	10	12	9	8	15	8	76
EXTERNAL FUNDING MNOK	7.2	21.9	22.5	36.0	34.0	32.1	26.7	30.0	26.9	237
MEDIA APPEARENCES	39	11	32	31	54	40	68	54	54	383

GENDER DISTRIBUTION
(HEADCOUNT)

MALE
FEMALE

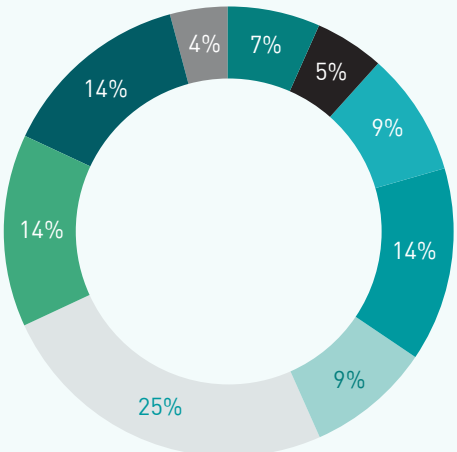
39%
61%

TOTAL: 223 PERSONS

Among the 223 persons involved in the CCBIO enterprise, there is a majority of women; of PhD students and postdocs well above 60% are female. The female share among senior scientific staff is steadily increasing year by year and is now on 48%. CCBIO's active recruitment of excellent female staff during its second CoE-period has increased the female part of its principal- and associate investigators to 31% by late 2021. CCBIO wishes to underline that no affirmative action has or will be taken at any point, since recruitment of faculty is done purely on merit, and among more junior staff and future group leaders also on perceived potential. By ensuring the available talent being put to its best use, CCBIO feels confident that the gender balance in its top tire will continue its upwards trend in the years to come.

CCBIO STAFF OVERVIEW
(HEADCOUNT)

PIS & ASS INV
PROF & ASS PROF
ADJUNCT PROF/RESEARCHERS
RESEARCHERS
POSTDOCS
PHD STUDENTS
STUDENTS
TECH STAFF
ADMIN STAFF

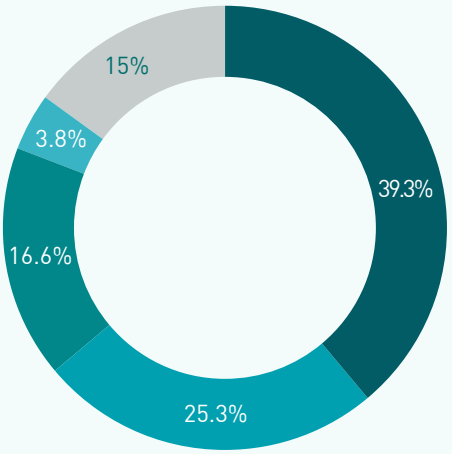


TOTAL: 223 PERSONS

CCBIO has a balanced composition of junior and senior researchers, technicians and engineers, and administrative support staff. To strengthen the ground for major breakthroughs and high-level publications, the center has decided to focus on recruiting postdocs rather than PhDs for the remainder of its CoE-period. CCBIO has also recruited younger, predominantly female, investigators as full- and associate PIs. Through the CCBIO Masterclass program, selected younger researchers receive targeted teaching and training to prepare them to become CCBIO's future group leaders. CCBIO's international network of 15 adjunct professors and researchers ensures excellent access to high-level collaboration, advice, and tuition for CCBIO's senior researchers, younger researchers, and PhDs.

FUNDING
(FUNDS USED IN 2021)

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

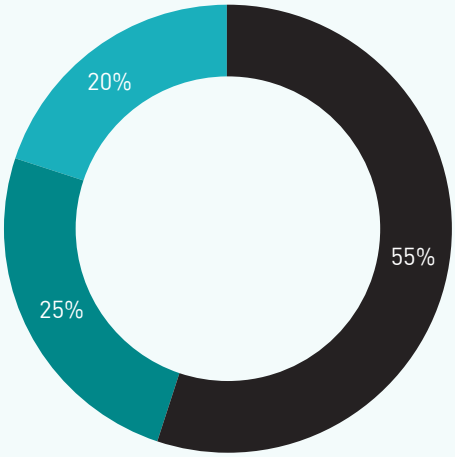


TOTAL: 76 MILL NOK

The pandemic related shutdown of laboratories and consumables crunch have had consequences far beyond the initial lockdown. This, in addition to cancellation of in-person meetings, naturally effected the rate at which funds were used in 2020 and 2021. We expect the consumption of financial resources to increase in step with CCBIO's effort to regain lost ground and the re-start of in-person events. Total funds used in 2021 were 76 MNOK, of which 25,3% is from the RCN CoE funding and 39% is own funding from the UiB. The external funding consumed was 35,4%, at 27 MNOK. Despite the slump in the actual use of funding, this is twice the budgeted amount and illustrates a high success rate with public and private funding agencies.

INTERNATIONALIZATION
(STAFF COUNTRY OF ORIGIN)

- NORWAY
- OTHER WESTERN COUNTRIES
- AFRICA & ASIA

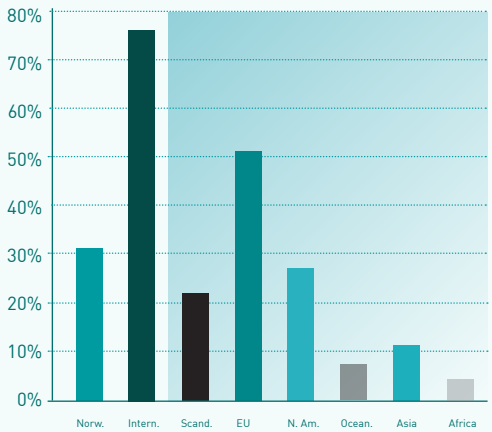


TOTAL: 223 PERSONS

Of CCBIO's overall staff, 45% have other citizenships than Norwegian, and 60% of its postdocs and 47% of PhDs originate from outside of Norway. In both of the latter categories, a clear majority of the international staff originate from Asia and Africa. Among CCBIO's senior researchers, 46% are foreign nationals. This makes CCBIO a truly international center of excellence.

INTERNATIONALIZATION
(STAFF CO-AUTHORSHIPS)

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



CCBIO's research is inherently international in nature and includes large international research networks. These networks, both formalized and publications based, have grown stronger and more integrated during CCBIO's CoE-period, generating an increasing number of scientific publications with international contributors. In 2021, 76% of CCBIO's publications had co-authors with their institutional affiliation abroad, a clear increase from 58% and 70% in 2019 and 2020 respectively. Notably, international co-authorships have much stronger prevalence than collaborations with researchers from other Norwegian universities (31%), and only 10% of publications are solely Bergen based. If we subdivide the international co-authorships into regions (grayed-out color), it is demonstrated that CCBIO collaborates with institutions from all major regions worldwide. If we add up the six columns to the right, we reach 122%. By comparing this total with the "International in aggregate"-category, one can deduce that most of CCBIO's international publications have co-authors from more than one region, being truly multilateral collaborations across several world regions.

COMMUNICATION AND DISSEMINATION 2021

COMMUNICATION AND DISSEMINATION

CCBIO aims to communicate and disseminate its findings to the public and continues to do this in a timely and informative way. In addition to publications and events for the scientific community, 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, presenting 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.

Examples of dissemination and communication efforts through social media in 2021:

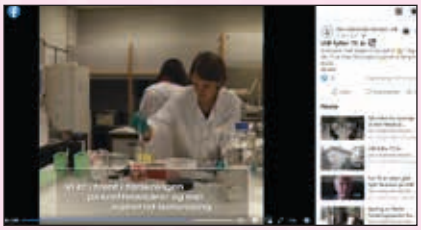
FACEBOOK entry on the 9th CCBIO Annual Symposium, focusing on top-notch speakers and that the symposium was fully digital this year.

FACEBOOK entry on the CCBIO/ Biomedicine course BMED904, for the first time held as an online event. Lab work is normally included in the course and was this time presented as how-to-videos.

FACEBOOK entry on CCBIO PI Camilla Krakstad who since November 2019 has been enrolled in the 12-Month Certificate Program Harvard Medical School Postgraduate Medical Education, High-Impact Cancer Research Program, and graduated in March with Top Honors (among the 5 best in the class of 2021), and with an award for best individual project.

FACEBOOK entry about CCBIO associate PI Ole Frithjof Norheim who was elected as a new member in The Norwegian Academy of Science and Letters. This institution, founded in 1857, is a non-governmental, nationwide body embracing all fields of research. Its main purpose is to support the advancement of research and scholarship in Norway. CCBIO associate PI Inge Jonassen was also elected as a new member, to group 8; Technology, class of Mathematics and Natural Sciences. Norheim was elected to group 3; Philosophy and Psychology, in the Humanities and Social Sciences class.

FACEBOOK entry on Hanna Kosberg Bredin, a third-year medical student in the Medical Student Research Program, who was awarded a NOK 40.000 scholarship from Sparebank1's Young Talents program. Hanna Bredin is affiliated to the Krakstad group, with Dr. Erling André Høivik as her supervisor.



FACEBOOK video published in occasion of the university's 75 years anniversary, showing CCBIO's work as one of the highlights in ongoing research.

TWITTER entry on a talk held by CCBIO's Director Lars A. Akslen and other CCBIO associates holding talks at the Mohn Medical Imaging and Visualization Centre (MMIV) conference on Precision Imaging Advancing Patient Care, December 2021.

TWITTER entry on the CCBIO Co-Director Bjørn Tore Gjertsen being awarded the prestigious King Olav V's Prize for Cancer Research 2021. The prize was presented by King Harald of Norway.

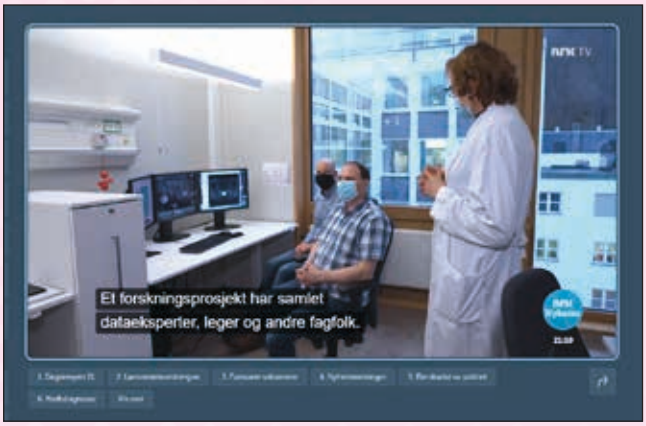
TWITTER entry commending the work of CCBIO PI Emmet McCormack and the support of NOK 8 million from the Norwegian Cancer Society for a project on immunotherapy development using new animal models. This year's allocation of funds from the Cancer Society also included CCBIO investigators Camilla Krakstad, Donald Gullberg and Lars A. Akslen, and postdoc Heidrun Vethe.

TWITTER entry on the TMS (Trond Mohn Foundation) Starting Grants to three deserving up-and-coming candidates, including Carina Strell for her project Understanding Early Breast Cancer Evolution in Space and Time (EvoMaps). Strell has since 2019 been affiliated to Uppsala University, Sweden. She has a long-term collaboration with Lars A. Akslen's group and her project will be embedded at CCBIO.

CCBIO has a unique dissemination effort in collaboration with the actor and molecular biologist Henriette Christie Ertsås, a CCBIO alumna. She offers interactive performances and lectures on cancer and biomarkers to schools on CCBIO's behalf. In 2021, 162 pupils in the Bergen area got to experience the tumor microenvironment on stage through 7 performances in schools in the open period between the COVID-19 lockdowns. Among these, 4 were booked through the annual Research Fair, which this year sent researchers out to visit schools instead of hosting a public event downtown, to comply with the pandemic measures. Henriette's lectures would also benefit an adult audience consisting of patients and relatives and can be employed to stimulate increased user participation in cancer research.

MEDIA APPEARANCES 2021

DECEMBER 25, 2021 - NRK
"For komplisert for legane: Slik skal kunstig intelligens oppdaga kreft" - Jone Trovik, Erling Høivik and Ingfrid Haldorsen (Krakstad group)



DECEMBER 20, 2021
- NRK DAGSREVYEN 21
"Kreftdiagnoser" - Jone Trovik, Erling Høivik and Ingfrid Haldorsen (Krakstad group)

DECEMBER 20, 2021
- NRK1 VESTLANDSREVYEN
"Bruker kunstig intelligens for å diagnostisere kreft" - Jone Trovik, Erling Høivik and Ingfrid Haldorsen (Krakstad group)

DECEMBER 14, 2021 - DAGENS MEDISIN
"Effekt av bemcentinib hos relapserende AML-pasienter" - Bjørn Tore Gjertsen


Dagens Medisin

Undersøker immunterapivaksine for AML-pasienter

DECEMBER 13, 2021
- DAGENS MEDISIN
"Undersøker immunterapivaksine for AML-pasienter" - Bjørn Tore Gjertsen


Medisin

Automatiserer mer av patologifaget

Ett av Norges største private medisinske laboratorier har tatt i bruk snittrobot og digital patologi. De nye teknikkene ved Førde Medisinsk Laboratorium kan revolusjonere patologifaget i Norge, mener patolog Ying Chen.

DECEMBER 7, 2021 - DAGENS MEDISIN
"Automatiserer mer av patologifaget"
- Ying Chen (Akslen group)


Medisin

To utfordringer for den nye helseministeren

Norge har fått ny helse- og omsorgsminister. Jeg vil gratulere Ingvild Kjerkol med jobben – og samtidig peke på to store utfordringer hun må ta tak i: Fastlegeordningen og persontilpasset medisin.

Ole Frithjof Norheim

VÅR PRIMÆRHELSETJENESTE er gutet i norsk helsetjeneste

NOVEMBER 9, 2021 - DAGENS MEDISIN
"To utfordringer for den nye helseministeren", Ole Frithjof Norheim

NOVEMBER 29, 2021 - BIOTEKNOLOGIRÅDET
"Podcast om Persontilpasset medisin og kreftbehandling" - Bjørn Tore Gjertsen and Eirik Tranvåg

NOVEMBER 24, 2021 - HEALTHTALK
"Ny Podcast: Knut Smeland er årets unge kreftforsker" - Line Bjørge


STUDVEST

Disse studentene vil forhindre en ny pandemi

Gjennom forskning vil studentene nå ta ansvar for at en fremtidig pandemi skal gå litt bedre.

NOVEMBER 2, 2021 - STUDVEST
"Disse studentene vil forhindre en ny pandemi" - Camilla Tvedt Ekanger (Lorens group)

MEDIA APPEARANCES

OCTOBER 18, 2021 - TV2 NYHETER
"Bjørn Tore Gjertsen ble tildelt Kreftforskningsprisen" - Bjørn Tore Gjertsen

OCTOBER 18, 2021 - ABC NYHETER
"Kongen tildelte Bjørn Tore Gjertsen kreftforskningspris" - Bjørn Tore Gjertsen

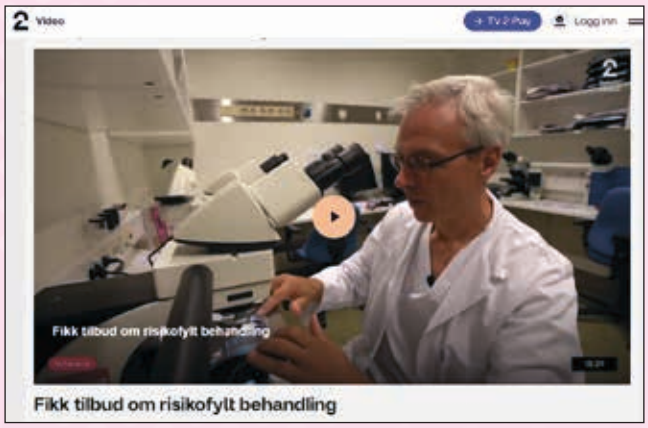
OCTOBER 18, 2021 - NORDRE
"Kongen tildelte Bjørn Tore Gjertsen kreftforskingspris" - Bjørn Tore Gjertsen

OCTOBER 1, 2021 - ONKOLOGISK TIDSSKRIFT
"Keytruda øker overlevelsen for pasienter med avansert livmorhalskreft" - Line Bjørge

SEPTEMBER 28, 2021 - UiO
"Former NCMM Associate Investigator awarded the King Olav V Cancer Prize"
- Bjørn Tore Gjertsen

SEPTEMBER 20, 2021 - UiB AKTUELT
"Henriette bruker teater for å formidle forskning" - Henriette Ertsås

SEPTEMBER 20, 2021 - TV2 NEWS
"Kjeld fikk aggressiv blodkreft - så kom redningen" - Bjørn Tore Gjertsen



SEPTEMBER 19, 2021 - TV2
"Fikk tilbud om risikofylt behandling"
- Bjørn Tore Gjertsen

SEPTEMBER 18, 2021
- DAGENS MEDISIN
"Tror på praksisendring for bruk av immunterapi ved livmorhalskreft"
- Line Bjørge

SEPTEMBER 19, 2021 - TV2 NEWS
"Overlege og professor Bjørn Tore Gjertsen vinner pris" - Bjørn Tore Gjertsen

SEPTEMBER 18, 2021 - DAGBLADET
"Rivende utvikling innen AML-medisiner"
- Bjørn Tore Gjertsen

SEPTEMBER 18, 2021 - DAGBLADET
"Bjørn Tore på sporet" - Bjørn Tore Gjertsen

SEPTEMBER 16, 2021 - DAGENS MEDISIN
"Store forventninger til årets europeiske kreftmøte" - Line Bjørge

SEPTEMBER 6, 2021 - NATIONEN
"Bjørn Tore Gjertsen tildelt Kreftforsknings-prisen for forskning på aggressiv blodkreft"
- Bjørn Tore Gjertsen

MEDIA APPEARANCES

SEPTEMBER 3, 2021 - FIRDAPOSTEN
"Bjørn Tore frå Florø får prestisjepris for verdsleiande kreftforsking" - Bjørn Tore Gjertsen

SEPTEMBER 2, 2021 - HEALTHTALK
"Kreftforskningsprisen til Bjørn Tore Gjertsen"
- Bjørn Tore Gjertsen


Adresseavisen NYHETSTUDIO NYHETER SPORT KULTUR DEBATT UKEADRESSA LOGG INN MENY

Bjørn Tore Gjertsen tildelt Kreftforskningsprisen for forskning på aggressiv blodkreft

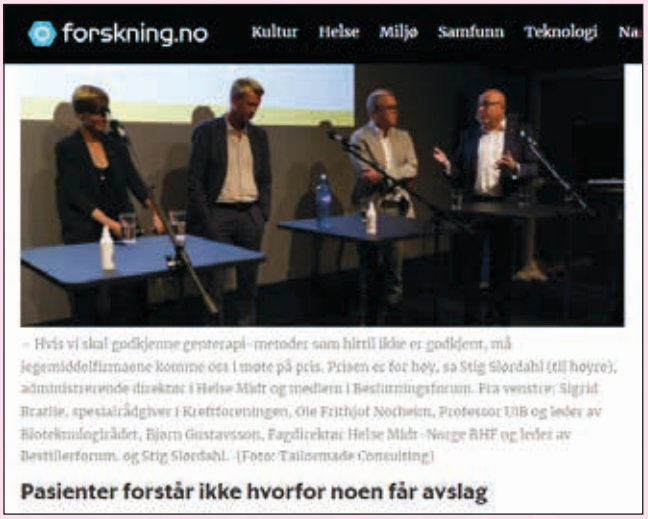
Professor Bjørn Tore Gjertsen tildeles Kong Olav Vs kreftforskningspris for sin verdensledende forskning på aggressiv blodkreft. Prisen er på én million kroner.

SEPTEMBER 2, 2021 - ADRESSEAVISEN
"Bjørn Tore Gjertsen tildelt Kreftforskningsprisen for forskning på aggressiv blodkreft"
- Bjørn Tore Gjertsen

SEPTEMBER 2, 2021 - AVISA MØRE
"Bjørn Tore Gjertsen tildelt Kreftforskningsprisen for forsking på aggressiv blodkreft"
- Bjørn Tore Gjertsen

SEPTEMBER 2, 2021 - DAGENS MEDISIN
"Haukelandsforsker får forskningspris" - Bjørn Tore Gjertsen

AUGUST 27, 2021 - DAGENS MEDISIN
"Slik kan genterapier få «ja» i Beslutningsforum"
- Ole Frithjof Norheim


forskning.no Kultur Helse Miljø Samfunn Teknologi Na

– Hvis vi skal godkjenne genterapi-metoder som hittil ikke er godkjent, må legemiddelfirmaene komme oss i møte på pris. Prisen er for høy, sa Stig Slørdahl (til høyre), administrerende direktør i Helse Midt og medlem i Beslutningsforum. Fra venstre: Sigrid Bratlie, spesialrådgiver i Kreftforeningen, Ole Frithjof Nolheim, Professor UiB og leder av Bioteknologirådet, Bjørn Gustavsson, Fagdirektør Helse Midt-Norge RHF og leder av Bestillerforum, og Stig Slørdahl. (Foto: Tailormade Consulting)

Pasienter forstår ikke hvorfor noen får avslag

AUGUST 24, 2021 - FORSKNINGNO
"Medisinsk genterapi hindrer alvorlig sykdom - hvorfor får ikke norske pasienter ta det i bruk?" - Ole Frithjof Norheim

AUGUST 19, 2021 - HEALTHTALK
"HealthTalk Debatten: Evaluering av nye metoder og medisinsk genterapi"
- Ole Frithjof Norheim

AUGUST 17, 2021 - MORNINGSTAR
"Papyrus Therapeutics Inc Announces Additions to Its Board of Directors"
- James Lorens

JULY 10, 2021 - NEWSWEB OSLO BØRS
"Preclinical bemcentinib and tilvestamab data presented at EAU 2021" - Jim Lorens

JUNE 11, 2021 - UiB AKTUELT
"Syv SFF-finalister fra UiB"
- Ole Frithjof Norheim/BCEPS

JUNE 25, 2021 - UiB AKTUELT
"Støtter 34 forskningsprosjekter ved UiB"
- Emmet McCormack and Camilla Krakstad

JUNE 25, 2021 - UiB AKTUELT
"Prisvinnere Fakultetets dag 2021"
- Ole Frithjof Norheim

JUNE 8, 2021 - HEALTHTALK
"Utfordrer Imbruvica: Calquence med færre kardiovaskulære bivirkninger"
- Bjørn Tore Gjertsen

JUNE 18, 2021 - DAGENS MEDISIN
"Post-ASCO: Siste nytt innen gynkreft"
- Line Bjørge

JUNE 4, 2021 - HEALTHTALK
"Tror kombinasjonen Venclyxto og azacitidin blir standardbehandling for pasienter som ikke kan motta intensiv cellegift"
- Bjørn Tore Gjertsen

MEDIA APPEARANCES

Milliondryss til innovasjoner ved UiB

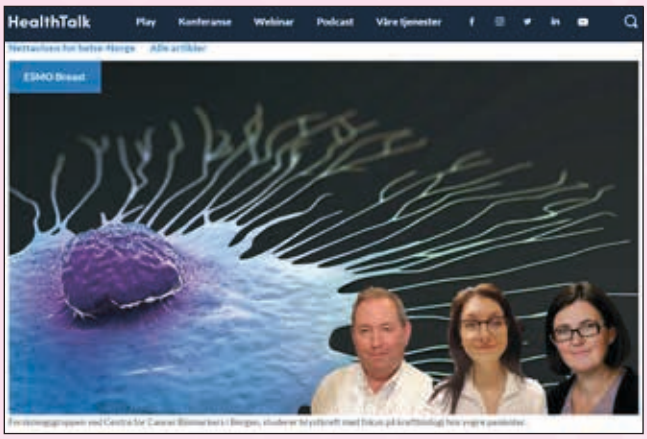
Universitetet i Bergen deler ut millioner til åtte innovasjonsprosjekter gjennom den nye satsingen for innovasjoner i tidligfase UiB idé.

Resultat av satsing på innovasjon

ÅRETS TILDELING

Årsutprosjekter:

MAY 20, 2021 - PÅ HØYDEN
"Milliondryss til innovasjoner ved UiB"
- Emmet McCormack



MAY 5, 2021 - HEALTHTALK
"Norske forskere har oppdaget en genmarkør med sterk prognostisk effekt ved brystkreft" - Lars A. Akslen, Elisabeth Wik, Lise Ingebriktsen

MAY 19, 2021 - DAGENS MEDISIN
"Stoppet studie viser effekt av immunterapi for livmorhalskreft-pasienter" - Line Bjørge

Karikerer kreftcellen

Som student fikk Henriette Ertsås ideen om å presentere forskning gjennom teater. I dag arbeider hun med formidling ved UiB.

APRIL 28, 2021 - PÅ HØYDEN
"Karikerer kreftcellen", Henriette Ertsås

APRIL 18, 2021 - NORD24
"- Enten blir det suksess - eller så blir det fiasko" - Nina Louise Jebsen (Gjertsen group)

APRIL 16, 2021 - AFRODITE MAGAZINE
"Ny studie på platinumresistent eggstokkreft"
- Line Bjørge

APRIL 13, 2021 - ROMSDALS BUDSTIKKE
"Talentstipend til Hanna (22) og to andre romsdalinger" - Hanna Kosberg Bredin (Krakstad group)

APRIL 12, 2021 - RBNETT
"Talentstipend til Hanna (22) fra Molde"
- Hanna Kosberg Bredin (Krakstad group)

APRIL 6, 2021 - PÅ HØYDEN
"UiB-professorer valgt inn i DNVA"
- Inge Jonassen and Ole-Frithjof Norheim

FEBRUARY 17, 2021 - PÅ HØYDEN
"UiB må fortsatt satse på fremragende sentre"
- Inge Jonassen

FEBRUARY 7, 2021 - ABC NYHETER
"Kreftceller kan gå i dvale og unngå cellegift. Nå vet forskere mer om hvordan de skal vekke og drepe dem" - Lars A. Akslen

MEDIA APPEARANCES

FEBRUARY 4, 2021 - DEUTSCHE WELLE
"Cancer research: Could drugs already on the market provide a cure?"
- Karl-Henning Kalland

FEBRUARY 1, 2021 - FORSKNING.NO
"Kreftceller kan gå i dvale og unngå cellegift. Nå vet forskere mer om hvordan de skal vekke og drepe dem" - Lars A. Akslen


Norske forskere utvikler fremtidens behandling:

NY METODE MOT FØFLEKK-KREFT

JANUARY 7, 2021 - VG
"Ny metode mot føflekk-kreft"
- Lars A. Akslen

MINI BIOGRAPHIES

PhD Candidates, Postdocs and Researchers 2021

ANANDAN, SHAMUNDEESWARI
MS in biotechnology and a PhD candidate in the Bjørge and McCormack groups until she completed her PhD in September 2021. Her PhD focused 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. Currently, she is working as a head engineer at Neuro-SysMed.

BAYSAL, EYLEM
MS in stem cell sciences from Hacettepe University, Turkey, and currently a PhD candidate at the Immune-Driven Regeneration research node at the Tissue Engineering Group and the Costea group. During her masters, Eylem examined the effect of melatonin on the Hippo signaling pathway in dental pulp stem cells. Her PhD project is focused on deciphering the molecular mechanisms involved in the crosstalk between regulatory T cells and bone marrow-derived mesenchymal stem cells in the context of bone regeneration.

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 immune responses, tumor-stroma crosstalk, and BRCA1 germline mutations, by using the imaging mass cytometry (IMC) Hyperion Imaging System.

BENTSEN, PÅL TORE
MD from the University of Bergen and currently a PhD candidate in the Gjertsen group. His research is focused on acute graft-versus-host disease (aGVHD) after allogeneic hematopoietic stem cell transplantation, with emphasis on corticosteroid 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, working on endometrial cancer. Her main focus is establishment of advanced preclinical model systems to improve our understanding of endometrial cancer biology and identify new therapeutic strategies.

BJØRNSTAD, OLE VIDHAMMER
MS in biomedicine from the University of Bergen and currently a PhD candidate in the Akslen 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.

BREMER, ANNE (NÉE BLANCHARD)
PhD in science and technology studies focusing 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 and 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 has co-edited the follow-up volume, to be published by Springer in 2022: "Precision Oncology and Cancer Biomarkers: Issues at stake and matters of concern".

BØRRETZEN, ASTRID
MD from the University of Bergen. She was a PhD candidate in the Akslen group (main supervisor Professor Ole J. Halvorsen) until she completed her degree in October 2021. Her research project focused on epithelial-mesenchymal transition, angiogenesis and molecular markers in aggressive prostate cancer.

CARRASCO, MANUEL
PhD from the Andalusian Molecular Biology and Regenerative Medicine Centre (CABIMER), focusing on how transcriptional networks control pancreas embryonic formation and adult pancreatic function. He thereafter did a postdoc at the University of Bergen, unveiling the importance of spatial organization to determine the mechanisms behind genetic diabetes. Carrasco is currently a researcher in the Akslen group, working with organoids as a model system for microenvironmental interactions in breast cancer, combining his experience as a developmental biologist and a pharmacist to understand mutual interactions between tumor cells and nerves in breast 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.

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
MDS in oral medicine and radiology from MCODS, Manipal University, Karnataka, India and BDS from BPKIHS, Nepal. 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 precursor lesions, particularly focusing on the prognostic significance of proliferation- and differentiation-related proteins in oral leucoplakia and oral squamous cell carcinoma.

DILLEKÅS, HANNA
PhD from the University of Bergen in 2020, focusing on tumor dormancy and how tissue trauma and wound healing can stimulate escape from dormancy to produce overt metastatic disease in breast cancer. She is currently a guest researcher in the Straume group and is coordinating the CCBIO Junior Scientist Symposia together with Maria Lie Lotsberg.

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. Since 2016 she is a PhD candidate in the McCormack and Gjertsen groups, focusing on development of a novel humanized bone marrow stem cell derived scaffold model in mouse. This bone marrow model will help to identify potential biomarkers, facilitating 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 at 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
PhD in bioinformatics from NTNU Norway, focusing on computational methods on gene regulation at the level of transcription. Currently he is a postdoc at the Computational Biology Unit (CBU) and CCBIO 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
PhD in biomedicine from the University of Bergen, focusing on intra-tumoral heterogeneity in glioblastoma and implications of immature phenotypes for tumor growth and resistance to treatment. Since 2013, she has been affiliated with CCBIO, first as a postdoc in the Lorens group, and later as a visiting researcher at the Gustave Roussy Cancer Center Grand Paris (France). 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.

ESPEDAL, HEIDI
PhD in neuro-oncology 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..

FORSSE, DAVID
MD, a gynecologist and a PhD candidate in the Krakstad Group until he completed his PhD in October 2021. His PhD work was on novel preoperative biomarkers and evaluation of altered treatment strategies to improve outcome for endometrial cancer patients, 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 the Kalland group, where he is involved in the development of cell-based therapeutic strategies for the treatment of cancer.

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 Bjørge 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.

GULATI, ANKUSH
MD and a specialist in Nuclear Medicine. Currently a PhD candidate researching on FDG-PET/CT of endometrial cancers as part of the Krakstad group at the Mohn Medical Imaging and Visualization Centre, including radiomics analysis.

GULLAKSEN, STEIN-ERIK
PhD from the University of Bergen in 2018 on single cell signaling and immune profiles in chronic myeloid leukemia. He is currently a researcher in the Gjertsen group, where his work revolves around single cell profiling of changes in immune cells 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.

HALLE, MARI KYLLESØ
PhD from the University of Bergen on molecular alterations suggesting new treatment strategies in uterine carcinomas. She is currently a researcher in the Krakstad group, working on gynecological cancer. Her main focus is to characterize targetable molecular alterations driving aggressive cervical carcinoma.

HUGDAHL, EMILIA
PhD from the University of Bergen focusing on biomarkers for aggressive cutaneous melanoma. She is currently working as a dermatologist at Bryggen Hudlegesenter and as a researcher in the Akslen group, exploring markers of immune cells and angiogenesis to define subgroups of aggressive melanoma using imaging mass cytometry (IMC).

HELLESØY, MONICA
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.

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

HUA, YAPING
PhD from the University of Bergen focusing 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 Kalland group, focusing on next generation AR modulators and STAT3 inhibitors in prostate cancer cells and therapeutic immune cells.

INGEBRIKTSEN, LISE MARTINE
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 was until 2021 a postdoc in the Krakstad group. Her research focused on molecular markers in endometrial cancer and their association with functional imaging parameters for individualized cancer treatment.

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

KALIYUGARASAN, SATHESHKUMAR
MS in Software Engineering from HVL and UiB, and currently a PhD candidate in the Krakstad group and the machine learning group at Mohn Medical Imaging and Visualization Center, Department of Radiology, Haukeland University Hospital. His PhD project is mainly related to machine learning and medical image analysis, with a particular focus on design methodologies in deep learning for efficient use of data with a special focus on gynecological cancers.

KJØLLE, SILJE
MS in molecular biology from the University of Bergen, and currently a PhD candidate in the Akslen group. Her research is focusing 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.

KANG, JING
MS in dermatology and venereology from Shandong University, and another MS in biomedicine from the University of Bergen. Until 2021 she was a PhD candidate in the Lorens group, focusing on the role of AXL signaling in cancer, with the overall aim to study TAM receptor dynamics in melanoma therapy resistance. She 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.

KLEFTOGIANNIS, DIMITRIOS
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 spatial analysis, combined with machine learning algorithms to gain insights into cancer progression mechanisms.

KLEINMANNS, KATRIN
PhD from the University of Bergen and currently a postdoc in the McCormack and Bjørge groups. Her research focuses on the development of immunocompetent patient-derived xenograft models of ovarian cancer to improve therapeutic interventions through novel immune therapies and targeted fluorescence image-guided surgery.

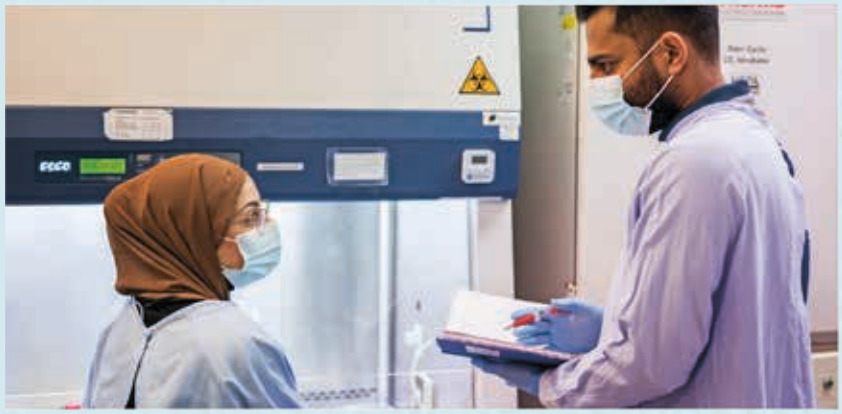
KLINGEN, TOR AUDUN
PhD from the University of Bergen focusing on vascular invasion by tumor cells and other prognostic factors in a population-based breast cancer study. He is currently senior consultant in pathology (Tønsberg) and a researcher in the Akslen group, focusing on immune cells and vascular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

KNUTSVIK, GØRIL
PhD from the University of Bergen focusing on biomarkers in breast cancer and in particular 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.

KTORIDOU-VALEN, IRINI
MD from the University of Semmelweis, Budapest. She joined the Gjertsen group in March 2021 as a PhD candidate, working on precision haemato-oncology. Her project focuses on biomarkers in the repurposing of known drugs for clinical trials for the treatment of acute myeloid leukemia.

LEITCH, CALUM
MS in molecular and cellular biology from the University of Glasgow. Throughout 2021 he was a PhD candidate in the Gjertsen group, aiming to defend in February 2022 with the project "Identification and development of small molecule therapies for the treatment of acute myeloid leukemia". His project focuses on the identification and repurposing of approved medicines for therapy development in AML, with particular emphasis on mechanistic studies to determine likely responders in patient sub-groups.

LELLAHI, SEYED MOHAMMAD
PhD from the University of Tromsø and currently a postdoc in the Kalland group, studying whether two dendritic cell subpopulations, conventional type 1 DCs and conventional type 2 DCs, are a better alternative for moDC in cryo-immunotherapy (CryoIT) treatment. He will also develop an "Organoid and DC co-culture model system" to study immune cells and cancer material in a more complex environment using the Hyperion Imaging System platform.



LIEN, HILDE
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 Krakstad group where she is using imaging mass cytometry to investigate tumor heterogeneity and prognostic markers in endometrial cancer.

LOTSBERG, MARIA LIE
PhD from the University of Bergen, focusing 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 the Lorens group, working on imaging mass cytometry and high dimensional analysis of the tumor microenvironment. She is also coordinating the CCBIO Junior Scientist Symposia together with Hanna Dillekås.

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, focusing on the cost-effectiveness of biomarkers in the Norwegian health care system and on the incentives of pharmaceutical companies to invest in R&D of drugs with companion biomarkers.

LURA, NJÅL GJERDE
MD with background in internal medicine and radiology. He is currently working on a PhD project in the Krakstad 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
PhD in bioinformatics from the University of la Réunion. She was a postdoc in Lorens' group 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.

MARIN, ORIOL CASTELLS
MS in biomedical research at the Pompeu Fabra University in Barcelona. He is currently a PhD student in the Gjertsen group. His project focuses on the immune analysis and signaling profiling of blood cells at a single-cell level by using mass cytometry. The aim is to assess mechanisms of response to treatment in acute myeloid leukemia clinical trials.

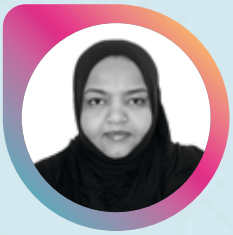
MATO, RAÚL PÉREZ
MS in molecular biomedicine from the Autonomous University of Madrid. Currently he is a PhD candidate in the Gullberg group. His PhD project deals with basic mechanisms occurring in the stromal compartment of the tumor microenvironment, focusing of integrin α11β1 as a regulator of interplay between tumor and stromal cells.

MESQUITA, ÂNGELA
MS in molecular genetics, and in health sciences, both from the University of Minho. Since October 2021, she is a PhD candidate in the Precision Oncology Research Group, under the supervision of Emmet McCormack and Dr. Pascal Gelebart. Her PhD research project focuses on the development new humanized mouse patient derived xenograft (PDX) models of myelodysplastic syndrome (MDS) to assess their ability to maintain the disease phenotype and cellular complexity for the pre-clinical evaluation of new innovative drugs.

MILOSEVIC, VLADAN
PhD in molecular medicine from the University of Turin, Italy, where he investigated the potential role of malignant pleural mesothelioma stem cells in the development of the chemo resistant and immune resistant phenotype of this highly aggressive tumor. He is currently a researcher in the Östman and Akslen groups, aiming to identify novel biomarkers and therapeutic targets of aggressive breast cancer through high-multiplex profiling of the tumor microenvironment using the Hyperion imaging mass cytometry platform.

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, focused on the expansion of mesenchymal stem cells under different expansion conditions. He is currently a PhD candidate in the Mustafa and Costea groups. His PhD project is focused on analysis of induced pluripotent stem cells generated from fibroblasts of different sources.

MOHAMED, NAZAR
PhD in oral sciences from the University of Bergen, focused on oral mycobiome in oral cancer as a source for prognostic biomarkers. Since June 2020 he is a guest researcher in the Costea group, working in multidisciplinary projects related to oral cancer, with specific focus on cancer microbiome.



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.

MUSTAFA, RAMMAH
MS from the Karolinska Institute within the Cancer Proteomics Group. He is currently a PhD candidate in the Costea and Bjørge groups and also collaborating with the Kalland group. Mustafa's project focuses on the exploration of innovative approaches for the establishment of patient derived organoid (PDO) models which can be used to predict drug response in vulva cancer by using mass cytometry (CyTOF).

MOTZFELDT, INGA KRISTINE FLAATEN
MS in Biomedicine from the University of Bergen, and a PhD candidate in the Gjertsen group. Her PhD project involves precision haemato-oncology and FLT3 mutations in acute myeloid leukemia. A specific focus is the biology connected to the various sequence lengths of the mutations, and how it affects response to targeted therapy.

MOUTOUSSAMY, EMMANUEL EDOUARD
PhD in molecular modeling from the University of Bergen. He is currently a researcher in the Lorens group. His research project is focused on the role of the receptor tyrosine kinase AXL in the context of cancer.

MUSIIME, MOSES
MS in biomedicine from the University of Bergen and a PhD candidate in the Gullberg group until he gained his PhD in September 2021. His PhD work focused on the role of integrin α11 in fibrosis and characterization of new tools for anti-fibrotic research. He is currently a postdoc in the same group, focused on the analysis of the cooperative roles of integrin α11 and syndecan-4 in fibroblasts using the fibrotic mouse heart as a model system.

NGINAMAU, ELISABETH SIVY
PhD in immunology from the University of Bergen focused on autoantigens in Sjögren`s Syndrome. 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
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 imaging mass cytometry (IMC) and 2-photon microscopy of living organisms.

PARAJULI, HIMALAYA
PhD from the University of Bergen focused on integrin α11 in oral carcinogenesis. He was a postdoc in the Thorsen Lab 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
PhD from the University of Bergen 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. He is currently working as consultant at the Department of Oncology, Haukeland University Hospital and is responsible as PI and co-PI in clinical studies in breast cancer and renal cancer in the Straume group.

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.

RAMNEFJELL, MARIA
PhD from the University of Bergen focusing 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 the Akslen group focusing on lung cancer biology, also collaborating with Dr. Agnete Engelsen.

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.

RANE, LALIT SHIRISH
PhD within immunology and IL-7 isoforms from the Karolinska Institute. 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.

RAYFORD, AUSTIN
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.

RØSLAND, GRO VATNE
PhD in molecular cell biology from the University of Bergen. Her PhD project focused on molecular mechanisms involved in glioblastoma progression, with an emphasis on stem cell markers and the epidermal growth factor system. As of 2021, she is a researcher in the Lorens group, where she works on AXL-mediated immunotherapy resistance, using high dimensional analysis tools and super resolution microscopy to characterize how AXL receptor signaling regulates tumor intrinsic resistance to immunotherapy.

SAND, LOUISE BERGSJØ
MS in chemistry from the University of Bergen and since August 2017 a PhD candidate in the in the Haug and McCormack groups 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
PhD on predictive markers in metastatic melanoma from the University of Bergen and Dr. Med from the Friedrich-Alexander University of Erlangen. She is currently 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. In 2020 and 2021 she also coordinated the CCBIO Junior Scientist Symposia together with Maria Lie Lotsberg.

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, focusing on the use of dendritic cells as a therapeutic option in the treatment of the myeloid malignancies.

SIRAJI, MUNTEQUA ISHTIAQ
MS in biomedical sciences from the University of Bergen and currently a PhD candidate in the Lorens group. His PhD project is titled "High-dimensional analysis of AXL-signaling in cancer therapy resistance". The rationale of the project is that understanding of the molecular mechanisms underpinning GAS6-AXL-mediated cell plasticity will offer unique therapeutic opportunities to improve cancer treatment

SLETTA, KRISTINE
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 was a PhD candidate in the Akslen group with Linda Stuhr as her main supervisor, until she completed her PhD in September 2021. Her project focused on the role of integrin α11β1 expression in breast cancer, in experimental models and in human breast cancer cohorts.

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.

TANDARIC, 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.

THOMSEN, LIV CECILIE VESTRHEIM
PhD from the University of Bergen focused on the genetic background of complex diseases. She is currently a researcher in the Bjørge group, also associated with the Gjertsen group. Her main research focus is on mass cytometry (CyTOF) analyses, developing 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.

TISLEVOLL, BENEDICTE SJO
MD from the University of Bergen. She is currently a PhD candidate in the Gjertsen group, focusing 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.

TORKILDSEN, CECILIE FREDVIK
MD from the University of Bergen. She is currently a PhD candidate in the Bjørge group. Her focus is on surgical management of ovarian cancer with the aim to identify clinical and molecular predictors of successful surgery.

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 UiB and a PhD candidate at the Bergen Centre for Ethics and Priority Setting (BCEPS) as part of CCBIO's ELSA team until he completed his PhD in September 2021 with Ole Frithjof Norheim as his main supervisor. His research focused on how cancer biomarkers can inform better and fairer priority setting decision and how personalized cancer medicine also may challenge the concept of fairness in priority setting. He now works as a senior advisor in the Norwegian Biotechnology Advisory Board.

VETHE, HEIDRUN
PhD from the University of Bergen on stem cells research and diabetes. She is currently a postdoc in the Akslen group, focusing on identifying protein biomarkers and novel targets in aggressive breast cancer, with 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 and a PhD candidate in the McCormack group until she completed her PhD in June 2021. Her research focused on the development and preclinical evaluation of site-specific dyes, allowing for accurate tumor development evaluation using optical and PET/CT imaging.

WAGNER-LARSEN, KARI STRØNO
MD and a PhD candidate in the Krakstad group, studying advanced MRI for developing more personalized treatment strategies in uterine cervical cancer. She is also a senior consultant in radiology at Haukeland University Hospital.

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 Krakstad group with Solveig Hofvind as her main supervisor. 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 2021

CCBIO – LIST OF PUBLICATIONS

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

Øvestad IT, Engesæter B, Halle MK, Akbari S, Bicskei B, Lapin M, Austdal M, Janssen EAM, Krakstad C, Lillesand M, Nordhus M, Munk AC, Gudlaugsson EG. High-Grade Cervical Intraepithelial Neoplasia (CIN) Associates with Increased Proliferation and Attenuated Immune Signaling. *Int J Mol Sci*. 2021 Dec 29;23(1):373. doi: 10.3390/ijms23010373. PMID: 35008799.

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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.

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Falch Lecture with Bob Langer (Video)

King Olav V's Prize for Cancer Research
(Bjørn T. Gjertsen).

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LIST OF PERSONNEL AT CCBIO 2021

Name	Position	Academic title	Group
Akslen, Lars A.	Professor, CCBIO director	MD, PhD	Akslen
Aljiafiri, Asia	Master student		Costea
Amant, Frédéric	Adjunct professor	MD, PhD	CCBIO
Anandan, Shamundeeswari	PhD candidate	MS, PhD	McCormack/Bjørge
Andresen, Vibeke	Senior researcher	MS, PhD	Gjertsen
Ardawatia, Vandana	Senior engineer	MS, PhD	Akslen
Arnes, Jarle Birger	Senior consultant	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 Programme	Stud.Med.	Kalland
Baysal, Eylem	PhD candidate	MS	Costea
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
Bergum, Brith	Senior engineer	MS, PhD	Core facility management
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
Bougnaud, Sébastien	Researcher	MS, PhD	Lorens
Bourdon, Jean-Christophe	Adjunct researcher	MS, PhD	CCBIO
Bozickovic, Olivera	Staff engineer	MS, PhD	Krakstad
Bredin, Hanna	Medical Student Research Programme	Stud.Med.	Krakstad
Brekken, Rolf	Adjunct professor	MD, PhD	CCBIO
Bremer, Anne Blanchard	Researcher	MA, PhD	Strand
Børretzen, Astrid	PhD candidate	MD, PhD	Akslen
Cairns, John	Adjunct professor	MA, MPhil	Health Economy
Carrasco, Manuel	Researcher	MS, PhD	Akslen
Chen, Ying	PhD candidate	MD	Akslen
Cleuren, Yamila Torres	Senior advisor	PhD	Administration
Costea, Daniela Elena	Professor	DDS, PhD	Costea
Dabija-Wolter, Gabriela	Associate professor	DDS, PhD	Costea
Das, Ridhima	PhD candidate	DDS	Costea
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	Guest researcher	MD, PhD	Straume
Disha, Nazia Islam	Master student		Gullberg
Dongre, Harsh	Postdoc	MS, PhD	Costea/Bjørge
Dowling, Tara Helen	PhD candidate	MS	Gjertsen/McCormack
Dugstad, Jenny Margrethe	Technician	MS	Krakstad
Dybvik, Julie	PhD candidate	MD	Krakstad
Dyrkolbotn, Kjetil	Senior executive officer	MA	Administration
Edelmann, Reidunn Jetne	Accociate professor	MD, PhD	Akslen
Ehsani, Rezvan	Postdoc	MS, PhD	Jonassen/Akslen
Eide, Agnes Jørgensen	Medical Student Research Programme	Stud.Med.	Krakstad
Ekanger, Camilla Tvedt	Master student		Lorens/Reed
Eldevik, Kristine Fasmer	PhD candidate	MS	Krakstad
Enge, Elisabeth	Study nurse		Krakstad/Bjørge
Engelsen, Agnete	Researcher	MS, PhD	Lorens
Espedal, Heidi	Postdoc	MS, PhD	Krakstad
Fagerholt, Oda Helen Eck	Medical Student Research Programme	Stud.Med.	Gjertsen
Fandalyuk, Zinayida	Staff engineer	MS	McCormack
Finne, Kenneth	Senior engineer	MS, PhD	Akslen
Fjeldstad, Karoline	Master student		Costea
Flatekvål, Helene Midtun	Head engineer	MS	Krakstad
Forsse, David	PhD candidate	MD, PhD	Krakstad
Fosse, Vibeke	Researcher, veterinarian	DVM	McCormack/Bjørge
Fromreide, Siren	Chief engineer	MS	Costea
Gabra, Hani	Adjunct professor	MD, PhD	CCBIO
Gabriel, Benjamin	Researcher	MS, PhD	Kalland
Gabrielsen, Tommy Staahl	Professor	MA, PhD	Health Economy
Gavasso, Sonia	Senior researcher	MS, PhD	Gjertsen
Gelebart, Pascal	Researcher	PhD	McCormack
Gissum, Karen Rosnes	PhD candidate	MS	Bjørge/Strand
Gjerde, Christiane Helgestad	PhD candidate	MD	Bjørge/McCormack
Gjertsen, Bjørn Tore	Professor, CCBIO co-director	MD, PhD	Gjertsen
Goni, Osman	Master student		Gullberg

Name	Position	Academic title	Group
Grigorian, André	Master student		Gullberg
Grøndal, Sturla Magnus	PhD candidate	MS	Lorens
Grønning, Mona	Chief engineer		Gullberg
Gulati, Ankush	PhD candidate	MD	Krakstad
Gullaksen, Stein Erik	Researcher	MS, PhD	Gjertsen
Gullberg, Donald	Professor	MS, PhD	Gullberg
Ha, Trung Quang	PhD candidate	MD, MS	Gjertsen
Haldorsen, Ingfrid Salvesen	Adjunct professor	MD, PhD	Krakstad
Halle, Mari Kyllesø	Researcher	MS, PhD	Krakstad
Halvorsen, Ole Johan	Professor emeritus	MD, PhD	Akslen
Hanif, Md Abu	Master student		Gjertsen
Harkestad, Kjetil	Senior executive officer		Administration
Hekland, Joakim	Master student		Lorens/Reed
Hellesøy, Monica	Postdoc	MS, PhD	Gjertsen
Hernandez, Inni Merete Offerdal	Senior executive officer		Administration
Hjelmeland, Marta Espevold	Master student		Krakstad
Hoang, Hua My	Staff engineer		Kalland
Hoang, Tuyen Thi Van	Head engineer	MS, PhD	Gjertsen
Hodneland, Erlend	Associate professor	MS, PhD	Krakstad
Hovland, Randi	Senior researcher	MS, PhD	Gjertsen
Hua, Yaping	Postdoc	PhD	Kalland
Hugdahl, Emilia	Researcher	MD, PhD	Akslen
Hugaas, Ulrikke	Medical Student Research Programme	Stud.Med.	Akslen (Wik)
Humlevik, Rasmus Olai Collett	Pre PhD candidate	MD	Wik/Akslen
Høgås, Mildrid Bønes	Senior executive officer		Administration
Høivik, Erling André	Researcher	MS, PhD	Krakstad
Ibrahim, Ahmed Eltayeb Ali	Guest researcher	DDS, PhD	Costea
Ingebriktsen, Lise Martine	PhD candidate	MS	Akslen (Wik)
Jacob, Havjin	Postdoc	MS, PhD	Krakstad
Jebsen, Nina Louise	Adjunct associate professor	MD, PhD	Gjertsen
Johannessen, Anne Christine	Professor	MD, DDS, PhD	Costea
Jonassen, Inge	Professor	MS, PhD	Jonassen
Kaliyugarasan, Sathiesh	PhD candidate	MS	Krakstad
Kalland, Karl-Henning	Professor	MD, PhD	Kalland
Kalvenes, Mai Britt	Senior engineer	MS, PhD	Akslen/Costea
Kang, Jing	Staff engineer	MD	Lorens
Kang, Jiyeon	PhD candidate	MS	Health Economy
Kimo, Magnus	Master student		Costea
Kjølle, Silje	PhD candidate	MS	Akslen
Kleftogiannis, Dimitrios	Postdoc	MS, PhD	Jonassen/Akslen
Kleinmanns, Katrin	Postdoc	PhD	McCormack/Bjørge
Klingen, Tor Audun	Researcher	MD	Akslen
Knutsvik, Gøril	Researcher	MD, PhD	Akslen
Kopperud, Reidun	Senior engineer	MS, PhD	Gjertsen
Krakstad, Camilla	Professor	MS, PhD	Krakstad
Ktoridou-Valen, Irini	PhD candidate	MD	Gjertsen
Kusche-Gullberg, Marion	Professor	MS, PhD	Gullberg
Kvamme, Amalie Bark	Medical Student Research Programme	Stud.Med.	Wik/Akslen
LaBarge, Mark	Adjunct professor	MS, PhD	CCBIO
Langer, Anika	Researcher	PhD	McCormack
Le, Minh Thu	Study nurse		Bjørge
Leitch, Calum	PhD candidate	MS	Gjertsen/McCormack
Lellahi, Seyed Mohammad	Postdoc	PhD	Kalland
Lien, Hilde Eide	PhD candidate	MS	Krakstad
Lindholm, Stein Rune	Research technician		Technical support
Litlekalsøy, Jorunn	Guest researcher	MS, PhD	Costea
Lode, Martine Rott	Master student	BS	McCormack
Lorens, James B.	Professor	MS, PhD	Lorens
Lotsberg, Maria Lie	Postdoc	MS, PhD	Lorens
Lu, Ning	Senior engineer	MS, PhD	Lorens/Gullberg
Luís, Ana Beatriz Mateus D'Avó	PhD candidate	MA, PhD	Health Economy
Lura, Njål Gjerde	PhD candidate	MD	Krakstad
Lyngstad, Jenny	Medical Student Research Programme	Stud.Med.	Krakstad
Løken, Geir Olav	CCBIO administrative leader	MA	Administration
Madeleine, Noëlly	Postdoc	PhD	Lorens
Madissoo, Kadri	Head engineer	MS	Krakstad
Mato, Raúl Pérez	PhD candidate	MS	Gullberg
McCormack, Emmet	Professor	MS, PhD	McCormack
Mesquita, Ângela	PhD candidate	MS	McCormack
Mills, Ian	Adjunct professor	MS, PhD	CCBIO
Milosevic, Vladan	Researcher	MD, PhD	Akslen

Name	Position	Academic title	Group
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Mohamed, Nazar	Guest researcher	DDS, PhD	Costea
Mohamed, Nuha Gafaar	PhD candidate	DDS	Costea
Motzfeldt, Inga Kirstine Flaaten	PhD candidate	MS	Gjertsen
Moutoussamy, Emmanuel Edouard	Postdoc	PhD	Lorens
Musiime, Moses	Postdoc	MS, PhD	Gullberg
Mustafa, Rammah	PhD candidate		Costea/Bjørge
Myrvold, Madeleine	Medical Student Research Programme	Stud.Med.	Krakstad
Neppelberg, Evelyn	Adjunct associate professor	DDS, PhD	Costea
Nginamau, Elisabeth Sivy	Researcher	MD, PhD	Costea
Nguyen, Rebecca	Lab technician		Gjertsen/Kalland
Nilsen, Irmelin Wilhelmsen	Guest researcher	M.Phil.	Strand
Norheim, Ole Frithjof	Professor	MD, PhD	Norheim
Omsland, Maria	Postdoc	MS, PhD	Gjertsen
Pantel, Klaus	Adjunct professor	MD, PhD	CCBIO
Parajuli, Himalaya	Postdoc	DDS, PhD	Costea
Peters, Stacey Ann D'Mello	Postdoc	PhD	Lorens
Pilskog, Martin	Researcher	MD, PhD	Straume
Poleo, Emilia Wold	Master student		Gjertsen
Pollard, Jeffrey	Adjunct professor	MS, PhD	CCBIO
Popa, Mihaela Lucia	Staff engineer, veterinarian	DVM	McCormack
Rajthala, Saroj	PhD candidate	MS	Costea
Ramnefjell, Maria	Researcher	MD, PhD	Akslen
Rana, Neha	PhD candidate	MS	Gjertsen
Rane, Lalit Shirish	Researcher	MS, PhD	Gjertsen
Rayford, Austin	PhD candidate	MS	Lorens
Reed, Rolf K.	Professor	MD, PhD	Reed
Riise, Julie	Professor	MA, PhD	Health Economy
Røsland, Gro Vatne	Researcher	MS, PhD	Lorens
Safont, Mireia Mayoral	Staff engineer	BS	McCormack
Salvesen, Gerd Signe	Staff engineer		Reed
Sand, Louise Bergsjø	PhD candidate	MS	McCormack
Schuster, Cornelia	Postdoc	MD, PhD	Akslen/Straume
Sefland, Øystein	PhD candidate	MD	Gjertsen
Sharmine, Shayla	Master student		Gjertsen
Siraji, Muntequa Ishtiaq	PhD candidate	MS	Lorens
Siyam, Diana	Medical Student Research Programme	Stud. Odont.	Costea
Skarsten, Gard Nærø	Master student		Lorens
Skavland, Jørn	Senior engineer	MS, PhD	Core facility management
Sletta, Kristine	PhD candidate	MS	Gjertsen
Smeland, Hilde Ytre-Hauge	PhD candidate	MS, PhD	Reed/Akslen
Solheim, Marion	Senior advisor		Administration
Stefansson, Ingunn	Professor	MD, PhD	Akslen
Stenmarck, Mille Sofie	Guest researcher	Cand.Med.	Strand
Stigen, Endre	Head engineer		Lorens
Strand, Roger	Professor	Dr.Scient.	Strand
Straume, Oddbjørn	Professor	MD, PhD	Straume
Strell, Carina	Adjunct researcher	PhD	CCBIO
Stuhr, Linda	Professor	MS, PhD	Reed
Suliman, Salwa	Senior researcher	DDS, PhD	Costea
Sværi, Bård Kjetil Bratli	Leading research technician		Technical support
Syrtveit, Astrid	Medical student		Wik
Sæle, Anna Kristine Myrmel	PhD candidate	MD	Akslen/Wik
Sørlie, Therese	Adjunct professor	MD, PhD	CCBIO
Tandaric, Luka	PhD candidate	MS	Bjørge/McCormack
Tegnander, Amalie Fagerli	Medical Student Research Programme	Stud.Med.	Akslen/Wik
Thakur, Dinbandhu	Master student		Costea
Thiery, Jean Paul	Adjunct professor	MD, PhD	CCBIO
Thomsen, Liv Cecilie Vestrheim	Researcher	MD, PhD	Gjertsen/Bjørge
Tislevoll, Benedicte Sjo	PhD candidate	MD	Gjertsen
Torkildsen, Cecilie Fredvik	PhD candidate	MD	Bjørge
Tornaas, Stian	PhD candidate		Costea
Tranvåg, Eirik Joakim	PhD candidate	MD, PhD	Norheim
Trovik, Jone	Professor	MD, PhD	Krakstad
Tveiterås, Maria	PhD candidate	MD, PhD	Reed
Van den Berg, Madeleine	Visiting student		Krakstad
Vethe, Heidrun	Postdoc	PhD	Akslen
Vidhammer, Eli Synnøve	Senior executive officer		Administration
Viñegra, Elvira García de Jalón	PhD candidate	MS, PhD	McCormack
Wagner-Larsen, Kari Strøno	PhD candidate	MD	Krakstad
Watnick, Randolph	Adjunct researcher	MD, PhD	CCBIO
Wik, Elisabeth	Associate professor	MD, PhD	Akslen/Wik
Willoughby, Robert	Master student	BS	McCormack
Winge, Ingeborg	Senior engineer	MS, PhD	Akslen
Wogsland, Cara Ellen	Senior researcher	PhD	McCormack
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	MS, MD	Krakstad

IN ZOOM

ANNUAL SYMPOSIUM MAY 19-20, 2021

INVITED SPEAKERS, AND CCBIO INVESTIGATORS AND ORGANIZERS

From the top left: Lars A. Akslen, Ulf Landegren, Lewis Au, Bjørn Tore Gjertsen, Klaus Pantel, Bernd Bodenmiller, Morag Park, Karl-Henning Kalland, Oddbjørn Straume, Ezra Cohen, Genevieve Boland, Camilla Krakstad, Liv Cecilie Vestrheim Thomsen, Hans Clevers, Else Driehuis, Jim Lorens, Rolf Brekken, Daniela Costea, Amir Aref, Geir Olav Løken, Eli Synnøve Vidhammer, Anil Sood, Jeffrey Pollard, Cornelia Schuster, Line Bjørge, Kara Davis, Hani Gabra, Agnete Engelsen, Elisabeth WiK

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