Centre for Cancer Biomarkers

Norwegian Centre of Excellence – University of Bergen

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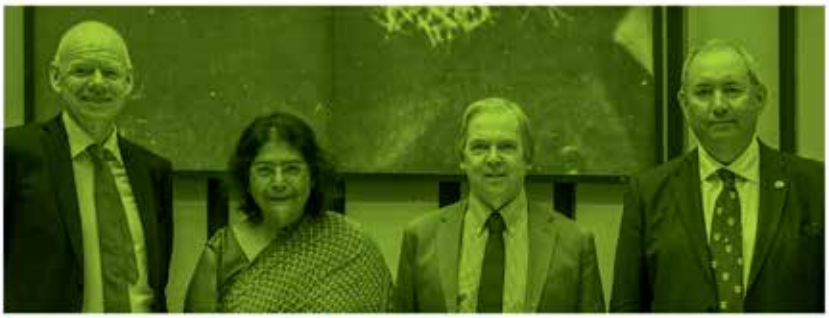

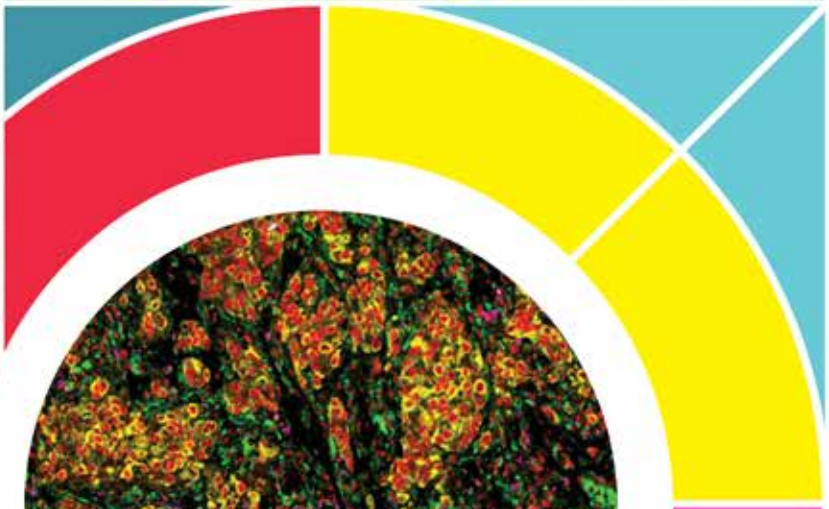

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ANNUAL SYMPOSIUM

ANNUAL REPORT

CONTENT

EDITORS: Lars A. Akslen, Geir Olav Løken, Eli Synnøve Vidhammer

PHOTOGRAPHERS: Thor Brødreskift, Ingvild Festervoll Melien, Gaute Hatlem, Geir Olav Løken, Eli Synnøve Vidhammer, Camilla Ekanger, Akslen group, Kalland group, McCormack group, Gjertsen group, Costea group, Strell group, Engelsen group, Anne Sidsel Herdlevær, Jørgen Barth, Elisabeth Wik, Mari Halle, Tarig Osman, Anne Blanchard, Axel Kirchoff/UKE, Luka Bertolaso, screenshots from Zoom and Microsoft Teams.

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DIRECTOR'S COMMENTS

CCBIO is now on the home stretch, and CCBIO 2.0 is rapidly approaching. Since being established in 2013, we have had 10 years with core funding from the Research Council of Norway to develop and nourish a Centre of Excellence with multifaceted activities in cancer biomarker research and contemporary precision oncology. While this first phase has been truly rewarding for all of us, the excitement and energy is now focused on the future. With key support from the University of Bergen and multiple external grants, we are entering the next phase on an optimistic note.

Throughout 2022, CCBIO has been in continuous motion with steady research activities and many efforts in science communication and education through the CCBIO Research School for Cancer Studies. We have a solid core curriculum of 12 courses relevant for researchers in biomarker studies, with translational and clinical extensions. The CCBIO Masterclass program, a year-long education of carefully selected top tier candidates (8-10) for mentoring and career planning, is now in its second cycle, and this concept has been very successful. Another innovation in 2022 is the CCBIO-ARC, or Advanced Research Colloquium, which is aimed to represent "food for thought" by monthly discussions within the PI-group of new concepts and key papers in biomedical research.

We are very thankful for the efforts of our International Faculty over the years, for their presence, advice, and collaborative input. CCBIO would not have been the same without the "extended family" of all these friends. We also thank our guests for the monthly research seminars, special seminars and courses during 2022 and in the past. During the *10th CCBIO Annual Symposium* in May, where we experienced a strong "get back" moment after the pandemic, we all felt the importance of coming together to enjoy each other's company and the fun of science. We had many strong presentations, and we will always remember and remain motivated by Bob Langer's fantastic journey in science and innovation.

Many important research papers have been published from CCBIO during the last year and are commented on elsewhere in this report. One of the latest highlights, presented in the 2022-2023 transition, is the recent work by Tislevoll et al. (Gjertsen group) published in Nature Communications. This elegant report demonstrates how single-cell signaling analytics by mass cytometry can allow for very early response prediction, eventually followed by treatment modification, in patients with acute myeloid leukemia. Importantly, the paper shows the significance of real-time functional diagnostics and adaptive therapy, a model that will now be pursued even for solid cancers. The related technique of single-cell studies by imaging mass cytometry (IMC), established by CCBIO and now used by many groups, is particularly promising for high-resolution biomarker mapping in tumor tissues. These mass cytometry approaches have been a strong strategic focus of CCBIO during the last 5 years.

Two books were published by CCBIO during 2022: Anne Blanchard and Roger Strand (eds): *Precision Oncology and Cancer Biomarkers: Issues at Stake and Matters of Concern* (Springer 2022), and Lars A. Akslen and Randolph S. Watnick (eds): *Biomarkers of the Tumor Microenvironment* (Springer 2022, 2. Ed.). Thank you to all contributors – many of them from CCBIO groups and networks.

One of the *hallmarks of CCBIO* has been to include studies on societal perspectives, with projects on ethical and economic topics – how to prioritize in a fair way, and how to understand our many efforts in a philosophical context. While we are focused on our individual projects and findings from day to day, we clearly need to widen our perspectives to see the "bigger picture" and reflect on the responsibility and long-term impact of what we do. To this effect, we have initiated a synthesis work on our outputs and outcome that can be observed over the years. This review will appear in a more detailed and mature form in our final report to be issued in 2024.

In this transitional period, we would like to quote Winston Churchill from 1942: *Now this is not the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning.* Said in a very different context, he also pointed out another deep truth that can be mentioned and remembered: *Success is not final, failure is not fatal, it is the courage to continue that counts.* To all the staff of CCBIO – thank you for all your hard work and for your courage and persistence. Let us keep up the pace and increase the momentum – together. ••

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 patients, 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 instruct 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)

ORGANIZATION OF THE CENTER

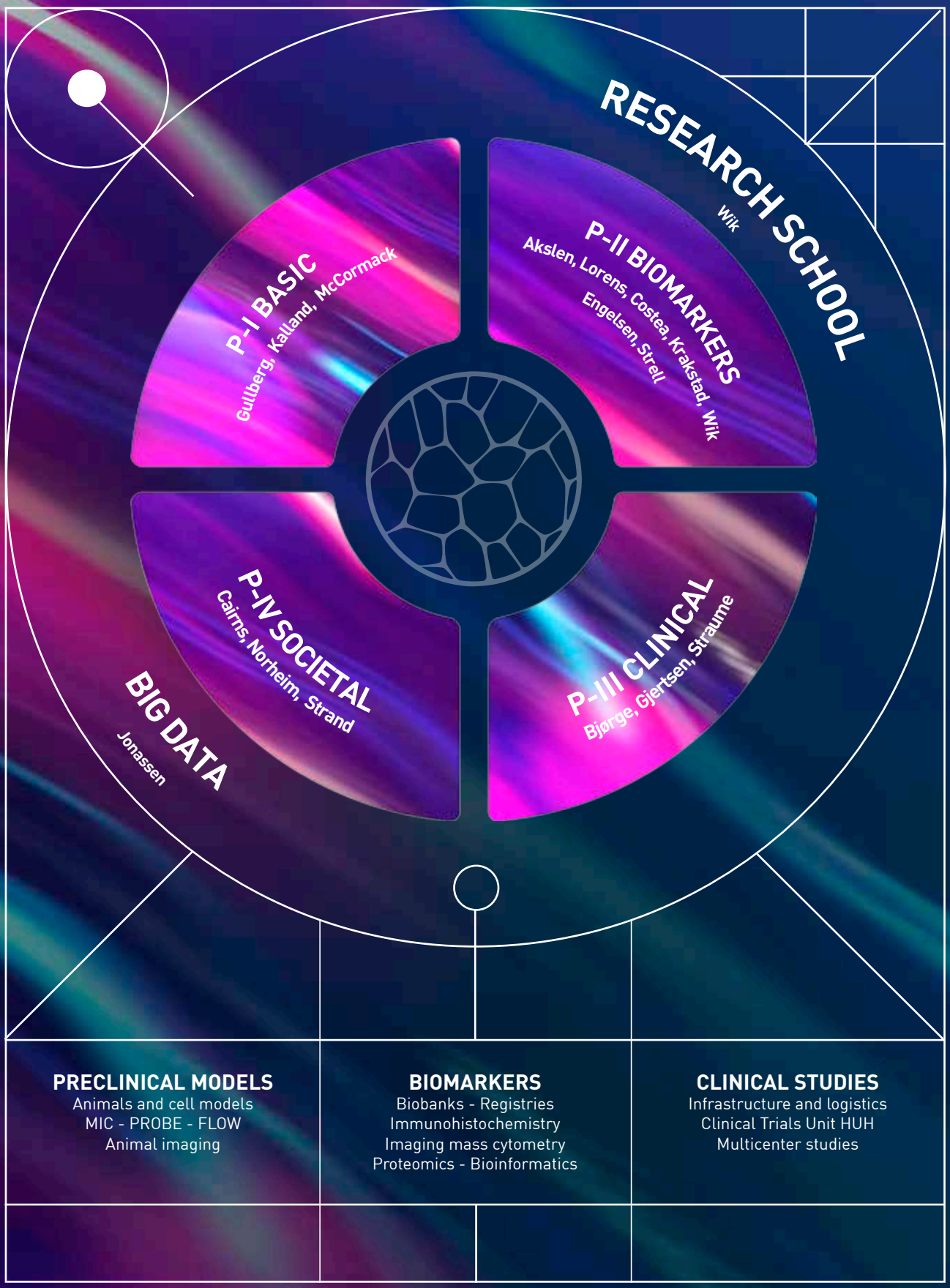
CCBIO is organized across seven departments and four faculties at the University of Bergen. Its main activities, with PIs, AIs and most of the other staff and equipment, are located at the Faculty of Medicine's Department of Clinical Medicine (CCBIO's host department), Department of Clinical Science,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

Management group
In 2022, CCBIO was managed by the director, Lars A. Akslen, the co-directors, Bjørn Tore Gjertsen and Line Bjørge, and the administrative leader, Geir Olav Løken. The management was 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), finance officers, the faculty communications officers and 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 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. ••


RESEARCH SCHOOL
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P-I BASIC
Gullberg, Kalland, McCormack
P-II BIOMARKERS
Akslen, Lorens, Costea, Krakstad, Wik
Engelsen, Strell
P-III CLINICAL
Bjørge, Gjertsen, Straume
P-IV SOCIETAL
Cairns, Norheim, Strand
BIG DATA
Jonassen
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: Rolf Brekken, CCBIO International Faculty

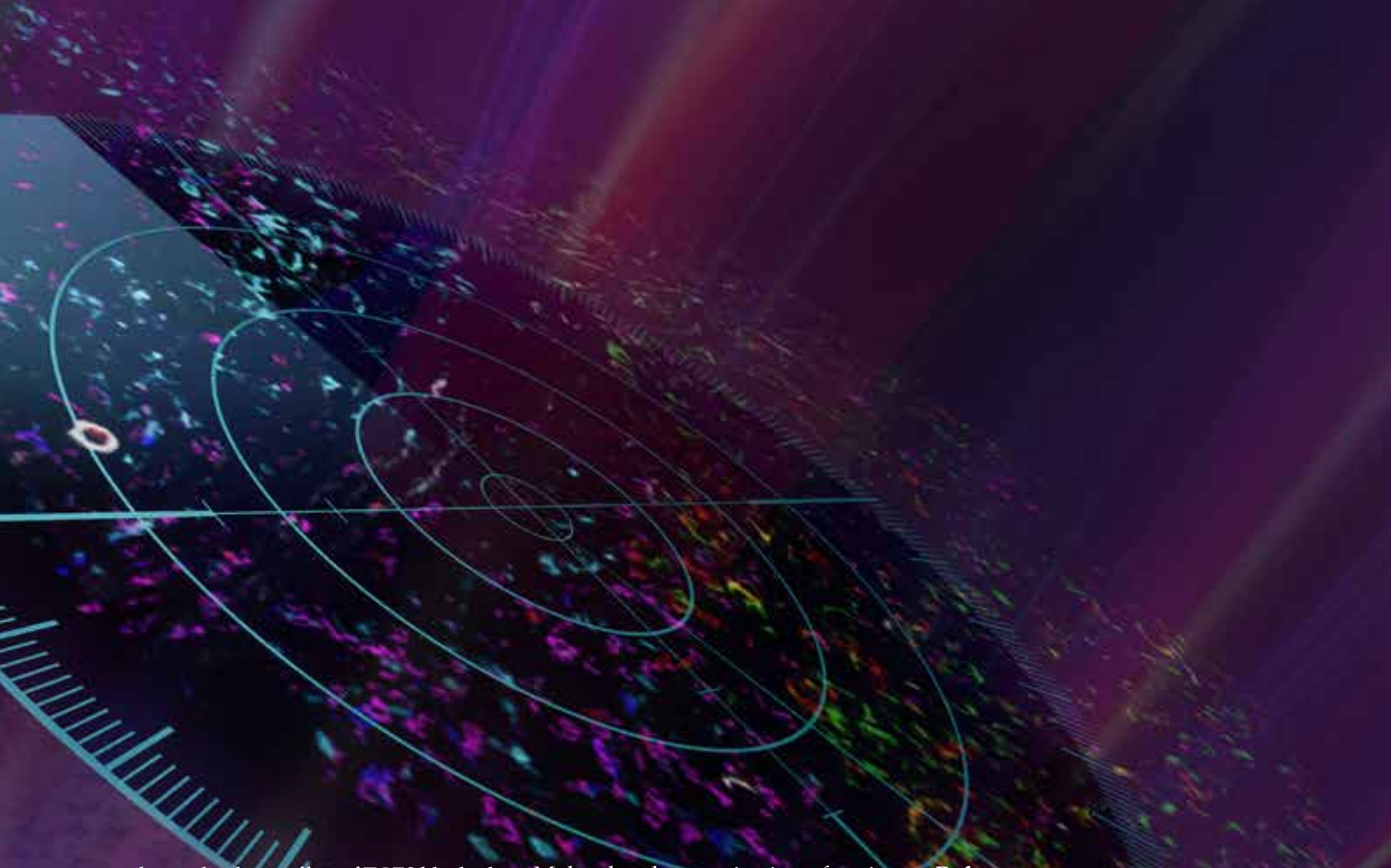
THE PROMISE OF PATIENT SELECTION IN TARGETING THE TUMOR MICROENVIRONMENT

The tumor microenvironment (TME) is a catch phrase that encompasses many aspects of tumor biology. Solid tumors consist of many cell types (e.g., tumor cells, immune cells, fibroblasts, endothelial cells) and an extracellular matrix that comprise the TME. Investigations into cell-cell communication and how cells in the tumor interact with and alter their local surroundings all fall under the umbrella of TME research. In general, an improved understanding of how the many facets of the TME contribute to tumor development and progression has elevated our ability to detect, diagnose and treat tumors. In fact, "targeting the TME" has become the strategy of the day in terms of developing new anti-cancer therapies. One needs to look no further than the explosion in therapeutic strategies that aim to harness the power of the immune system for cancer therapy. Immune oncology approaches capitalize on the TME by altering signaling between tumor cells and the microenvironment to facilitate immune recognition and immune-mediated destruction of tumor cells.

A particularly potent immune oncology strategy is immune checkpoint blockade (ICB). Immune checkpoints are evolutionarily conserved "OFF" signals designed to constrain the duration and amplitude of T cell-mediated immune responses to reduce collateral tissue damage and maintain self-tolerance. Tumors hijack immune checkpoints as a major strategy to avoid immune surveillance. Thus, blockade of immune checkpoints can release tumor antigen primed T cells to attack tumor cells. This has been effective in a subset of cancer patients; however, a significant portion of cancer patients do not benefit or only have partial or short-term responses. The "rules" that dictate response to ICB are being re-evaluated on a regular basis but it is clear that tumor antigen primed effector T cells are required for ICB to be effective.

Appropriately primed effector T cells are often lacking in solid tumors. This is due in part to the TME, in which there are many mechanisms, pathways and cell types that induce and maintain an environment that suppresses the development and recruitment of primed effector T cells. Thus, targeted agents that inhibit TME-related signaling are being combined with ICB in preclinical and clinical studies. However, given the numerous TME associated pathways that can contribute to the deficit of effector T cells, it is unlikely that a single TME pathway or target will have broad spectrum efficacy in combination with ICB.

An attractive idea is to identify patients based on *oncogenotype* and pair TME-targeted therapy with an appropriate ICB based on biology. Two examples from our preclinical experience follow. First, transforming growth factor β (TGFβ) is a major driver of immune suppression and epithelial plasticity and consequently is an attractive therapeutic target in many solid tumors. However, TGFβ is also a tumor suppressor. As a result, blocking TGFβ has not been effective preclinically or clinically thus far in unselected patient populations. Importantly, mutations in the canonical TGFβ signaling cascade are common in some cancers. For instance, loss of TGFβ receptor 2 or Smad4 occurs frequently in pancreatic cancer. We found that *TGFβ receptor 2-deficient* pancreatic tumor cells form tumors that are sensitive to TGFβ inhibition (Huang et al., 2019). Current unpublished studies support that pancreatic tumors that are *Smad4-deficient* also respond positively to TGFβ blockade. Efficacy in each case is



due to the direct effect of TGFβ blockade on the TME. Furthermore, inhibition of TGFβ in these TGFβ-signaling deficient tumors results in a substantial change in the tumor immune landscape portending an improved response to ICB. These observations suggest that patients with a deficiency in canonical TGFβ signaling should be considered for TGFβ inhibition while patients that are wild-type for TGFβ signaling should not be enrolled in studies that exploit a TGFβ-targeting strategy. A second example of targeting a TME pathway in a distinct oncogenotype can be drawn from studies performed in *LKB1/Stk11* mutant lung cancer, an oncogenotype that is typically refractory to ICB. Inhibition of the receptor tyrosine kinase AXL on stromal cells, in particular dendritic cells, facilitates the development of tumor antigen primed effector T cells resulting in tumor sensitivity to ICB. AXL can also be expressed on the tumor cell but does not appear to be relevant to the increase in response to ICB in this scenario; highlighting that TME associated AXL is the critical target (Li et al., 2022).

These examples demonstrate the utility of linking tumor cell oncogenotype to distinct TME-targeting strategies. Molecular characterization of patient tumors is becoming routine in the clinical decision tree of cancer care. Understanding how particular oncogenotypes influence the TME should be the next wave of TME research. To that end, a recent study on a novel $Kras^{G12D}$ inhibitor, MRTX1133, demonstrates that efficacy in pancreatic cancer models relies on T cells (Kemp et al., 2023). These data suggest that combining MRTX1133 with the appropriate TME-targeted agent has the potential to provide long-term benefit in a historically recalcitrant tumor. Until recently, "targeted therapy" has been limited to pharmacologic inhibition of specific alterations in tumor cells. It is time to broaden that definition to include identifying targets in the TME of selected patients. Linking distinct oncogenic drivers to TME-associated, pharmacologically targetable vulnerabilities is a significant undertaking, but has the potential to deliver the next wave of precision medicine: patient selection for rationally designed combination therapy. ••

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CCBIO Opinion

Text: Frédéric Amant, CCBIO International Faculty

HOW TO EFFICIENTLY ORGANIZE TRANSLATIONAL CANCER RESEARCH?

Today, my lab of Gynecologic Oncology at the Catholic University Leuven hosts 2 senior researchers, 2 postdoctoral researchers with a Marie-Curie fellowship, 12 PhD students, 2 lab techs and 3 master students. Though this lab is a modest player in the field when regarded from an international perspective, it may be inspiring to look at its evolution. Indeed, its constitution strongly contrasts with that in 2002, when I was the first and only PhD student in this field.

What could have been key in this evolution?

Get inspired. In 2004, when I met a patient that was diagnosed with cervical cancer during pregnancy, there appeared to be a complete lack of prospective studies. Moreover, this topic was not in the portfolio of any research group. Fellow clinicians and researchers considered cervical cancer too uncommon to invest time and resources in. For me, it was a unique opportunity to make a difference, not only for the patients but also to fill the research gap. There was little to lose. Furthermore, holding a degree in 'Obstetrics and Gynecology' with a sub-specialization in 'Gynecologic Oncology', I found myself uniquely positioned to link both 'cancer' and 'pregnancy' themes. Our first paper on the safety of applying chemotherapy during pregnancy[1], changed the paradigm and proved that chemotherapy can be given safely during pregnancy. Likewise, when founding Trace – a platform of patient-derived preclinical models that I created in 2013 to study cancer biology and resistance to treatment – I found my inspiration at the patients' bedside. Thus, close interaction between clinicians and scientists is pivotal to identify clinical needs and link these to research options.

Focus. When resources are limited, straddling research topics are to be avoided. It is then advised to focus on achieving preliminary results in order to convince funders, *e.g.* grant organizations, to award the necessary financial means allowing you to further enroll the research line. Yet, the challenge is to find the right balance between keeping this focus and adopting an open attitude towards new and unannounced opportunities harboring promising research avenues. Furthermore, patience is the partner of focus. For instance, the time gap between the first steps in our search for metabolomic changes contributing to platin resistance in ovarian cancer and the first report[2], surpassed 7 years.

People management. A strong team relies on the presence of experts (to be) in your research domain and recruiting these profiles is a first step. Ideally, these experts are (to become) better than yourself. Their excellence will best thrive when they are given sufficient freedom. For us, it works best when, together with the team members, we outline the main research paths. From this point on, their expertise and experience will guide them towards the next steps. Trust and confidence will (mostly) be rewarded with team members who are flourishing.

Teamwork. Conducting research is a team effort. Attention to a good team spirit is a daily task and starts with a 'good morning', also to the janitor. A personal interest in your team members adds to their self-confidence, paving the

way to partnership rather than being in a subordinate role. Prevention of absenteeism and burn-out is a positive side effect of this approach, yet it is not a goal on its own. Likewise, teambuilding efforts will only generate its beneficial effect if they are rooted in a safe environment.

As can be appreciated from the above, the efficient organization of a translational research lab is a work in progress. Also, luck has its role and there are no guarantees for success. Moreover, no perfect situation exists, since diverse issues, like events happening in the private sphere, underperformance of team members, missing necessary financial grants, and administrative issues can interfere with the perfect road map. In sum, striving towards the best together with your team will generate a fertile soil where ideas can sprout and be converted into projects. And, in case the research output would be less than hoped for, being able to work in a positive, supportive and warm environment is already a gift to care for.

Good luck.

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CCBIO Opinion

Text: Karen Rosnes Gissum, Line Bjørge & Roger Strand, CCBIO

LIVING WITH OVARIAN CANCER: TRANSITIONS LOST IN TRANSLATION

Ovarian cancer is a serious and highly lethal disease. For most women, it is a disease they have never heard of until they are diagnosed with it, making it difficult to understand and accept. Vague symptoms of illness suddenly become translated into a medical diagnosis, and although the disease will be treated, if not cured, the experience of illness will remain.

Women's experiences of and perspectives on illness and disease change along with their cancer trajectory. They experience losing their identity, not recognizing the *I in me*, not knowing who they are (Gissum et al., 2022). Women tell stories of being alone with the illness and disease, protecting their close ones from what they describe as torture, observing that the experience of illness at some point overcomes the disease itself. Being between illness and disease is to be lost in translation between the two worlds of ovarian cancer.

Medical advances in precision oncology, the increased reliance on genomic data, the use of biomarker testing, and patients' varying psychological responses have complicated the communication regarding precision oncology and personalized medicine. Although cancer is a medically definable physical disease, cancer – like many other diseases that threaten life and health – has also been commonly used as a symbol. Symbols or metaphors are integral parts of everyday language and thinking. Metaphors may help patients control their thoughts and feelings about their illness and allow them to share their thoughts and feelings with others. In a patient–physician relationship, symbols of disease can help build a foundation for common clinical understanding. However, the horizons of patients and physicians are different, and the gap between the biomedical world and the *life-worlds of patients* is large. The more complex the scientific advances, the more space should be given to patients to voice what disease and illness mean to them.

In the last decade, there has been an increase in the number of clinical trials focusing on biomarkers that can prolong the lives of patients with ovarian cancer, but few trials have concentrated on how biomarkers can be used to establish individual follow-up care for ovarian cancer patients, and little attention has been paid to the ethical aspects of participating in such clinical trials. What patients want for their lives, how they want to manage their disease and their experience of illness, how they communicate their suffering, and how communication issues may influence their decision-making and informed consent to participate in the trials should be crucial considerations in the era of precision oncology, with the goal of improving the quality of life of patients with ovarian cancer. ••

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CCBIO Opinion
Text: Line Bjørge, CCBIO co-director

PROMISES AND PROBLEMS OF PRECISION ONCOLOGY

Since 1999, when the foundation document for precision medicine was published[1], the term precision oncology has been used to substantiate the importance of genomic information for risk assessment, diagnosis, and treatment selection in cancer.

Increasingly more genomic tests are being conducted in clinical practice. As early as 1998, the BCR-ABL rearrangement in chronic myeloid leukemia was shown to be successfully targeted with imatinib. In 2012, an anti-tumor activity of the poly (adenosine diphosphate [ADP]–ribose) polymerase (PARP) inhibitor in patients with ovarian cancer with BRCA1/BRCA2 mutations was shown. Additionally, over the years, non-small cell lung cancer has emerged as an architype for genomic data use for optimal treatment selection throughout the treatment course. The introduction of genomic testing is both resource intensive and expensive, and as usage increases, a multidisciplinary decision-making approach is required. The introduction of more and more targeted drugs on the market will further increase the complexity.

The concept of precision oncology was introduced with the hope that it could radically change patient management. However, more than two decades after its introduction, the approach has not, with a few exceptions, lived up to expectations. Hopefully, the different ongoing drug rediscovery initiatives that redefine approved drug use beyond their labels to patients with potentially actionable variants, will represent a move forward.

Due to decades of scientific work and technical innovation, the molecular understanding of tumor biology has advanced. Clearly, the prospects of precision oncology depend not only on genomic data in a static map but also on biological real-time understanding of spatial resolution and interrogation of cell–cell interactions to deliver the right treatment to the right patient at the right dose and at the right time. Spatial omics and multiplexed imaging are needed to explore cancer subclones and/or molecular biomarkers within their native spatial contexts. Technologies that allow the integration of multi-omics data are being developed. Once in place, the full potential of molecular profiling and precision oncology will be evident. Interestingly, all approaches used today to determine treatment response are based on tumor load and do not generate functional parameters about therapy effects. Notably, the use of single-cell signaling profiling and machine learning approaches to identify predictors for 5-year overall survival 24 hours after the first chemotherapy cycle in acute myeloid leukemia patients was recently demonstrated[2]. Functional diagnostics providing "next generation biomarkers" are necessary to generate this real-time information and algorithms to discriminate between therapy responders and non-responders, allowing early therapy adjustments in models for adaptive and precise treatment. ••

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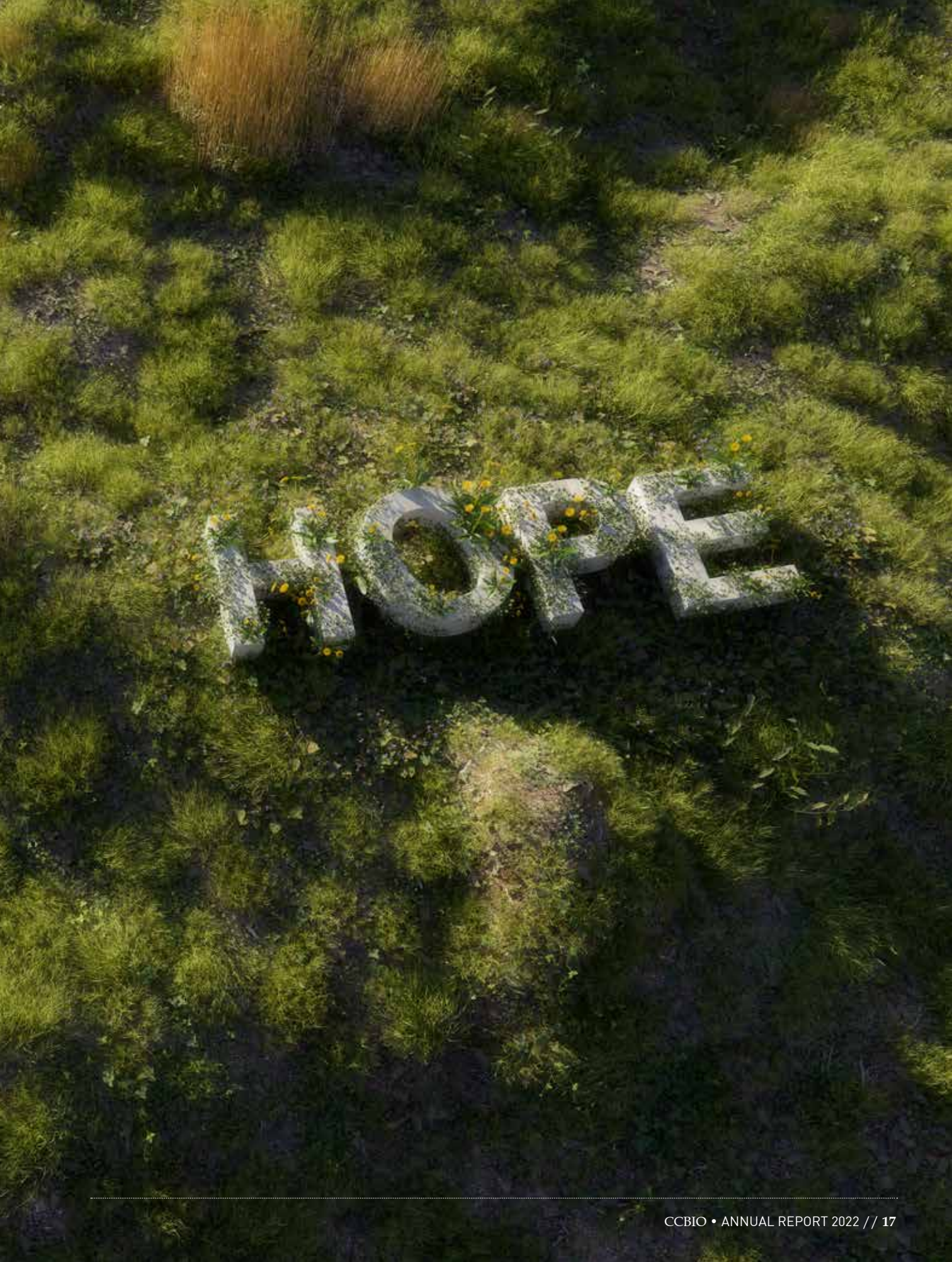

HOPE

SCIENTIFIC ACTIVITIES AND PROGRESS 2022

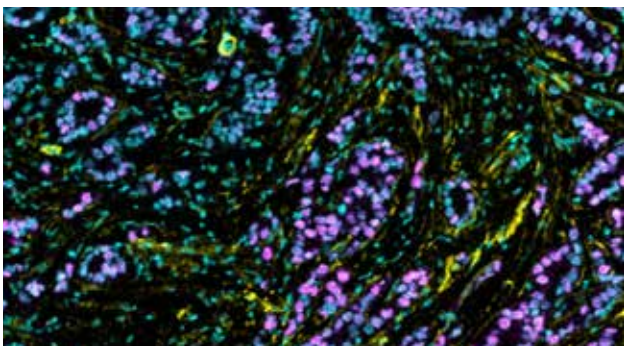
CCBIO has a two-armed program of biomedical (Team 1-3) and societal (Team 4) projects. The center has a focus on cancer mechanisms and biomarkers related to tumor-microenvironment crosstalk in primary and metastatic lesions, with increasing use of single-cell analytics and functional profiling of cells and tissues. The center concentrates on how biomarkers can delineate aggressive tumor phenotypes and predict tumor progression and therapy response. Societal studies of ethics, economics, priorities, and philosophy represent integrated aspects 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 2022, our activities were still influenced by COVID recovery and rebound effects following the pandemic. Laboratories have been up and running although with some delays on the delivery side. Whereas courses and meetings were mostly back to "on site" mode, some of the knowledge and skills gained through this period will forever be part of our new routines. The "get back" moment at the CCBIO Annual Symposium in May was striking.

Our research activities were progressing steadily with significant output and emerging ideas for new studies. The CCBIO Research School for Cancer Studies has a stable core curriculum with 12 credit giving courses and a range of activities. The 1st CCBIO Masterclass for career development was an important program for 8 selected candidates (2021-2022), and the second group of 10 candidates is now ongoing (2022-2023). The INTPART-II grant from the RCN enhances our international networking and the relationship with our strong partner - the Vascular Biology Program at Boston Children's Hospital and Harvard Medical School.

In **TEAM 1,** projects are focusing on how tumor cells interact with and instruct their surrounding 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.

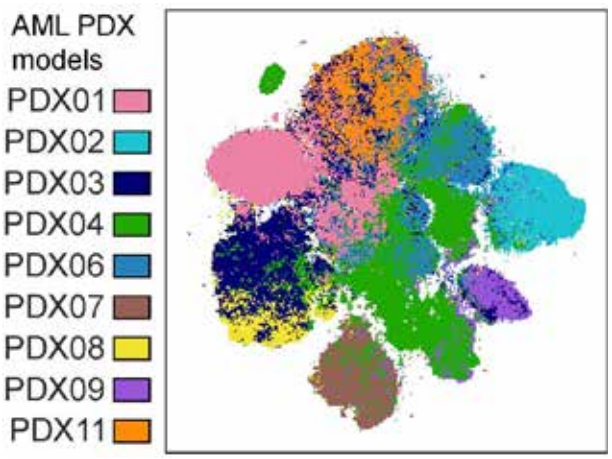
The **Gullberg group** has been working on fibroblast biology and the importance of integrin α11 in the tumor microenvironment, by the characterization of novel integrin α11 function blocking antibodies and development of a mouse model to explore the role of α11 in tumor stroma. Establishing the ITGA11-Cre mouse strain was a major milestone in the group's work after 10 years of focused efforts. The further breeding into a fluorescent reporter strain will be another step forward. The detailed epitope mapping of mAb 210F4 and mAb 203E1 to a few amino acids also illustrates the importance of consistent work spanning several years to reach long-lasting and well-cited results. One of the translational projects 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).



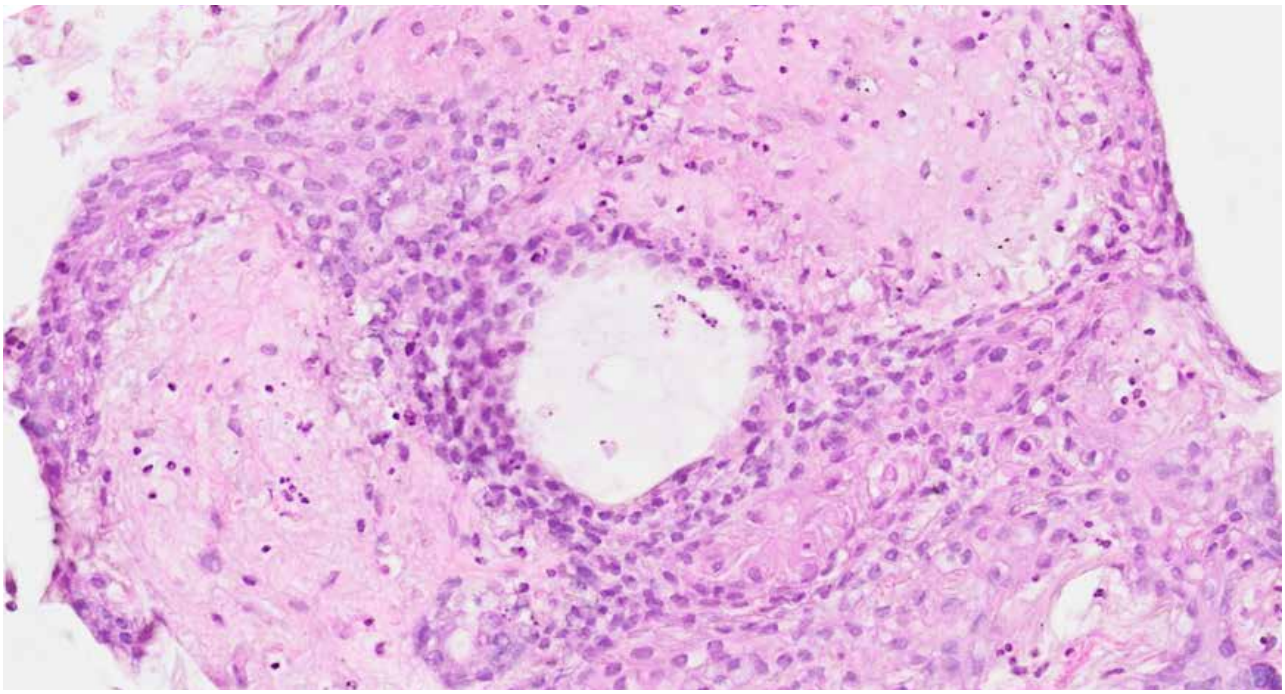
In the **Kalland group**, focus has been on two strategies: drug discovery by repurposing, and the concept of cryoimmuno-based dendritic cell (DC) therapy. In a phase I clinical trial for cryoimmuno-therapy (CryoIT) for patients with advanced prostate cancer, immature DCs are placed in the inflammatory cryoablated prostate cancer tissue to 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 (Thomsen et al., *Cancer Immunol Immunother*, in press). The group continues to explore biomarkers in order to uncover positive 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 (fall 2023). Work is ongoing to secure and improve the manufacturing practice of DCs with optimal and robust operating procedures, to secure potency and viability. The role of beta-catenin and STAT3 signaling in dendritic cell re-programming are also studied (Azeem et al., *Biomedicines* 2021). Notably, the European Patent Office has approved the patent application of CryoIT combined with intratumoral injection of an immune checkpoint inhibitor. The national implementation phase is ongoing.

The **McCormack group** has had a major focus on appropriate preclinical models (organoids, PDX) before clinical trials are performed. In 2022, the group's intrabursal orthotopic PDX model of ovarian cancer – critical to the development of personalized therapies in this disease – was presented in detail (Popa et al., *Methods Mol Biol* 2022). Kleinmanns et al. (*Cancers* 2022) described, for the first time, the development and application of a humanized orthotopic PDX model of high-grade serous ovarian cancer. In this work, Kleinmanns reported the parameters necessary to develop such a model, extensive functional analysis of humanization with CyTOF (34 markers), and application with anti-PD-1 inhibition. The group surveyed the use of preclinical modelling systems within academia and industry (Fosse et al., *J Pers. Med* 2022). Subsequently, Fosse leads a team of internationally recognized scientists to establish guidelines for robust and reproducible preclinical research in personalized medicine (Fosse et al., *BMC Med* 2023). The group has several biomarkers under development as novel targets for CAR-T, which will be developed in their novel immunocompetent PDX models.



In **TEAM 2**, studies are being performed on biomarker discovery and validation in several human tumors, with additional work on how markers are related to mechanisms for tumor progress, especially within the tumor microenvironment. Candidate biomarkers are used to map tumor diversity including associations with clinico-pathologic phenotypes and patient outcome.

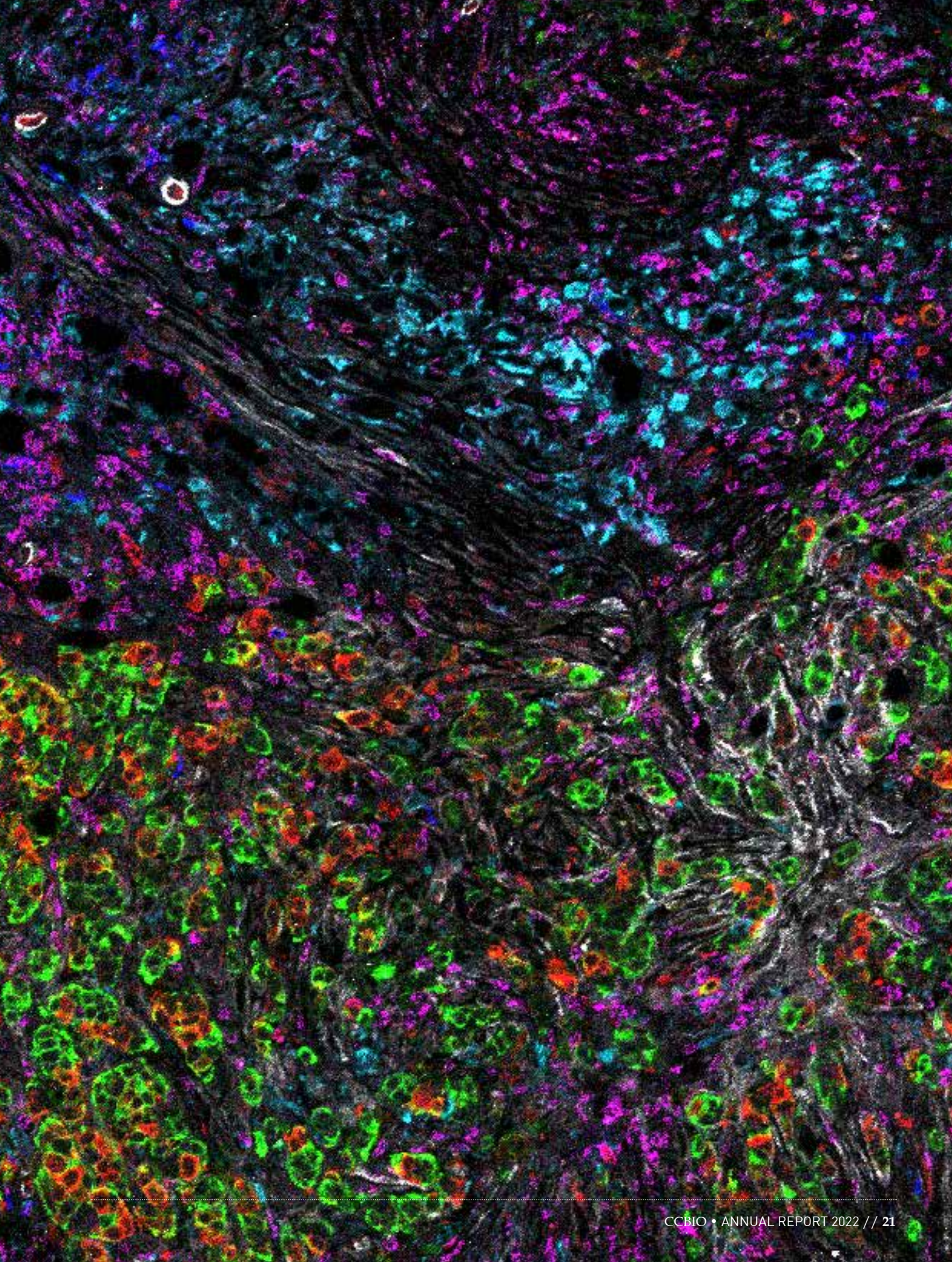


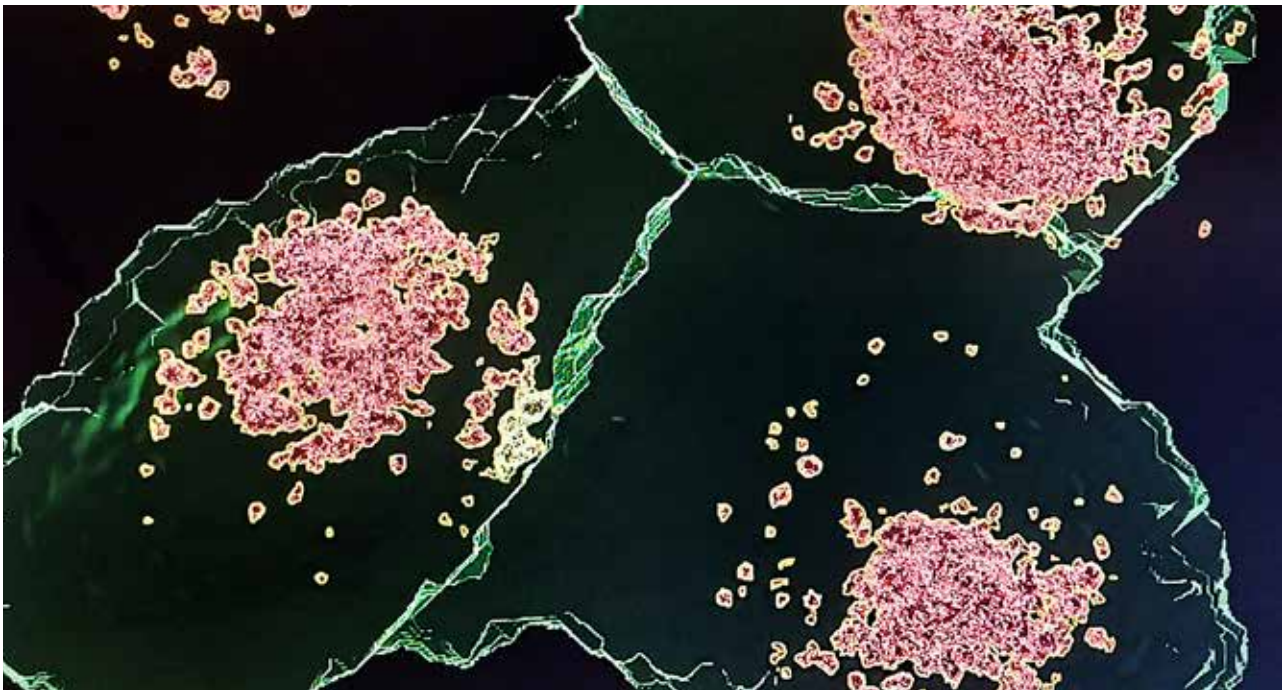
The **Akslen group** is concentrating on tumor proteomics and spatial mapping of tissue biomarkers related to the tumor microenvironment in human breast cancer (BC). The overall aim is to improve tumor stratification and treatment response prediction. The focus is currently on profiling of luminal-like and basal-like breast tumors, using mass spectrometry proteomics (MSP) and imaging mass cytometry (IMC). During 2022, the group identified a stromal proteomic signature which could improve BC stratification, in particular among luminal tumors (Finne et al., submitted). By integrating BC cell line secretome data after hypoxia with stromal proteome information, significantly improved prognostic information and potential treatment predictive ability was found (Kjølle et al., in revision). The group also found that neurogenesis and angiogenesis are linked in aggressive breast cancer (Wik et al., submitted) and that co-cultivation of BC cells and neural cells leads to proteomic responses in both cell populations (Bjørnstad et al., submitted). In a study of breast and prostate cancer, the group recently reported, in collaboration with Drs. Watnick and Brekken, that PRSS2 and TSP1 interactions could influence programming of the tumor-immune microenvironment (Sui et al., *Nat Commun* 2022). The expression patterns of Stathmin in relation to immune cell populations in breast cancer has been studied by single-cell spatial mapping, supporting an immune regulatory role (Askeland et al., in preparation).

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. Results have indicated an important role of Axl in epithelial-mesenchymal transition (EMT) and immune evasion (Engelsen et al., *Front Immunol* 2022), and studies have demonstrated how anti-Axl treatment (by bemcentinib) can reverse these processes. Thus, in a study of STK11/LKB1 mutant lung cancer (NSCLC), the team reported that AXL targeting can restore PD-1 blockade sensitivity (Li et al., *Cell Rep Med* 2022).

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 has presented data on miRNA profiling in head and neck cancer and found 12 differentially expressed miRs. Two of the significantly downregulated miRNAs in CAF, miR-204 and miR-138, have tumor-suppressive function through inhibition of fibroblast migration by modulating the expression of several different motility-related molecules (Rajthala et al., *Int J Mol Sci* 2021; Rajthala et al., *Front Oncol* 2022). A link between miR-204 and integrin α11 was found, and in a cohort of 169 patients with HPV-negative primary oral squamous carcinoma, stromal presence of miR-204 predicted better overall and recurrence free survival (Rajthala et al., *Cancers* 2021).

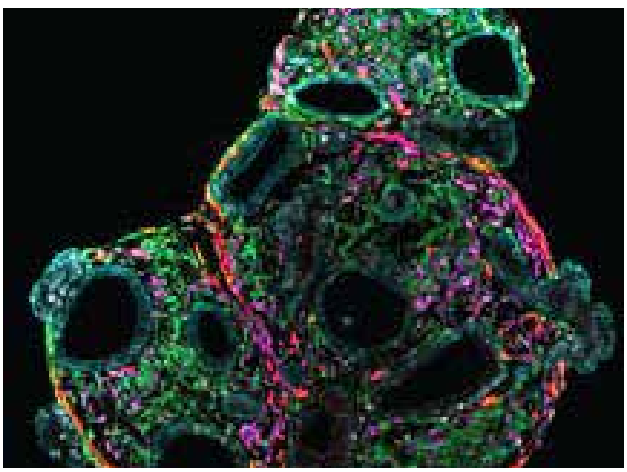
The **Engelsen group** has focused on how phenotypic plasticity interferes with therapeutic efficacy and immune cell-mediated killing. The group has now established lung cancer (NSCLC) patient-derived organoid and explant models recapitulating the complex tumor-immune microenvironment, and the current project aims to elucidate the effect of phenotypic plasticity on the spatial organization of tumor-immune microenvironment. This might illuminate how therapeutic targeting of phenotypic plasticity and intermediate E/M



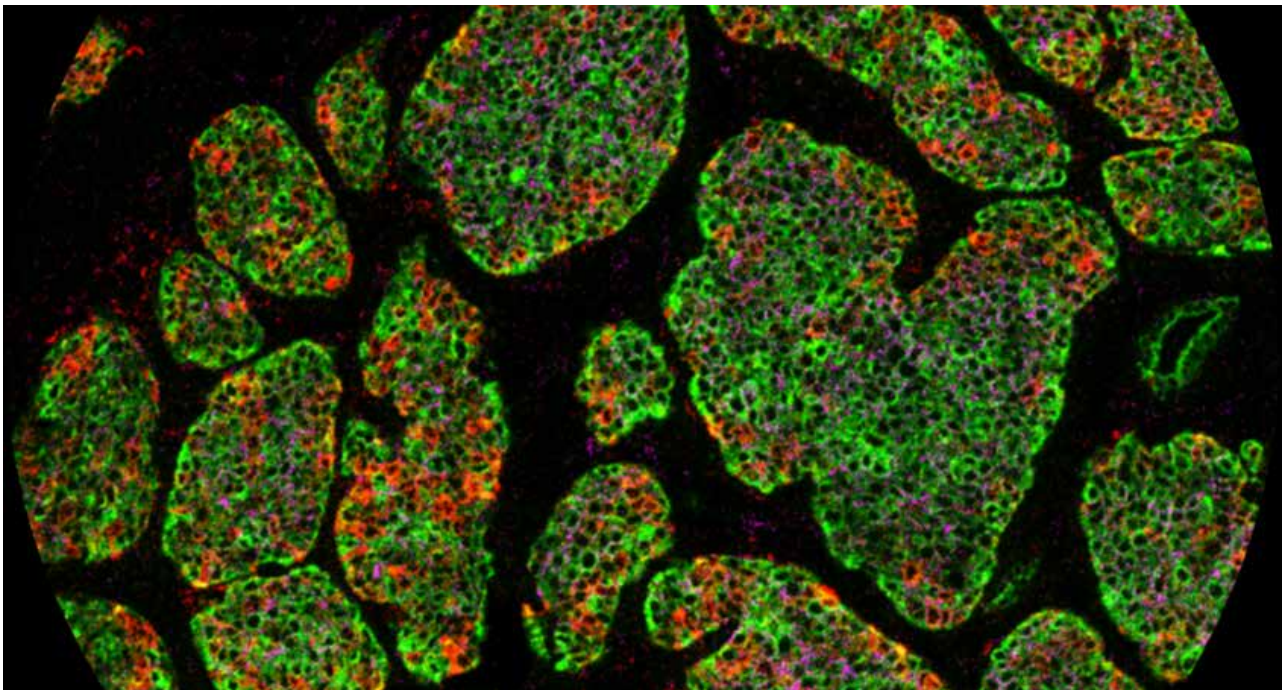


phenotype cells synergize with immune checkpoint inhibition (ICI) therapy. Recently, the team reported how organoid and immune-competent explant models can be applied to explore how hypoxia and therapeutic interventions alter the cancer cell metabolism and the tumor-immune microenvironment (Zaarour et al., *Cancers* 2021; Engelsen et al., *Front Immunol* 2022). Also, tumor-stroma interactions in lung cancer were reported by spatial mapping using heterotypic spheroid models (Lotsberg et al., *Front Oncol*, 2022).

In studies of gynecologic cancers by the **Krakstad group**, tissue and serum-based biomarkers as well as genetic alterations are being explored. The international MOMATEC2 study (NCT02543710), a phase 4 implementation trial for validation of ER/PR status to stratify for lymphadenectomy in endometrial cancer, is coordinated by the group. Models for endometrial cancer are being established and characterized, and integration of molecular and radiologic data with clinical phenotypes is ongoing. In a study investigating MMR status in paired preoperative and operative endometrial cancer biopsies, the group demonstrated a substantial agreement in MMR status between paired lesions (Berg et al., *Br J Cancer* 2022). In addition to determining MMR status, protein expression levels for MMR, particularly MSH6, may add prognostic information in endometrial cancer. Patients with endometrial cancer undergoing lymph node staging (LNS) without receiving chemotherapy are comparable with those not undergoing LNS (Forsse et al., *Am J Obstet Gynecol* 2022). The team found similar diagnostic performance in the low- and high-risk histology groups for central staging parameters by preoperative MRI and FDG-PET/CT (Fasmer et al., *Eur Radiol* 2022). Selective [18F]FDG-PET/CT in patients with high-risk MRI findings yields better detection of lymph node metastases than MRI alone, and similar diagnostic performance to that of MRI and [18F]FDG-PET/CT in all.



The **Strell group** studies regulatory mechanisms of early breast cancer evolution with focus on genetic alterations and changes in the tumor microenvironment. The group aims to identify novel prognostic and predictive biomarkers which can support clinical decisions. Strell joined CCBIO during 2022 after receiving a starting grant from the Trond Mohn Foundation for the project *EvoMaps – understanding early breast cancer evolution in space and time*. Strell has been working on spatial tissue profiling techniques in Stockholm and Uppsala (Svedlund et al., *EBioMedicine* 2019; Micke, Strell et al., *EBioMedicine* 2021). Previous work in the Mats Nilsson group (Science for Life Laboratory, Stockholm University) in collaboration with Lucy Yates (Wellcome Sanger Institute) has demonstrated a base

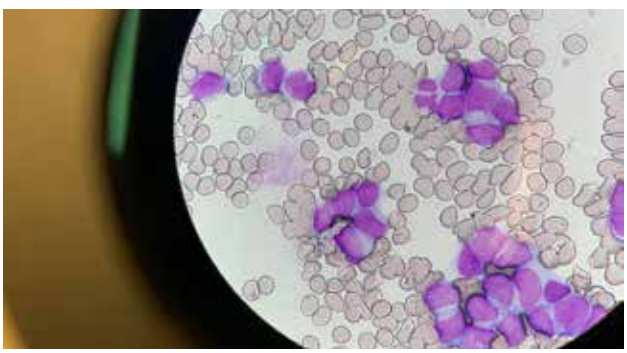


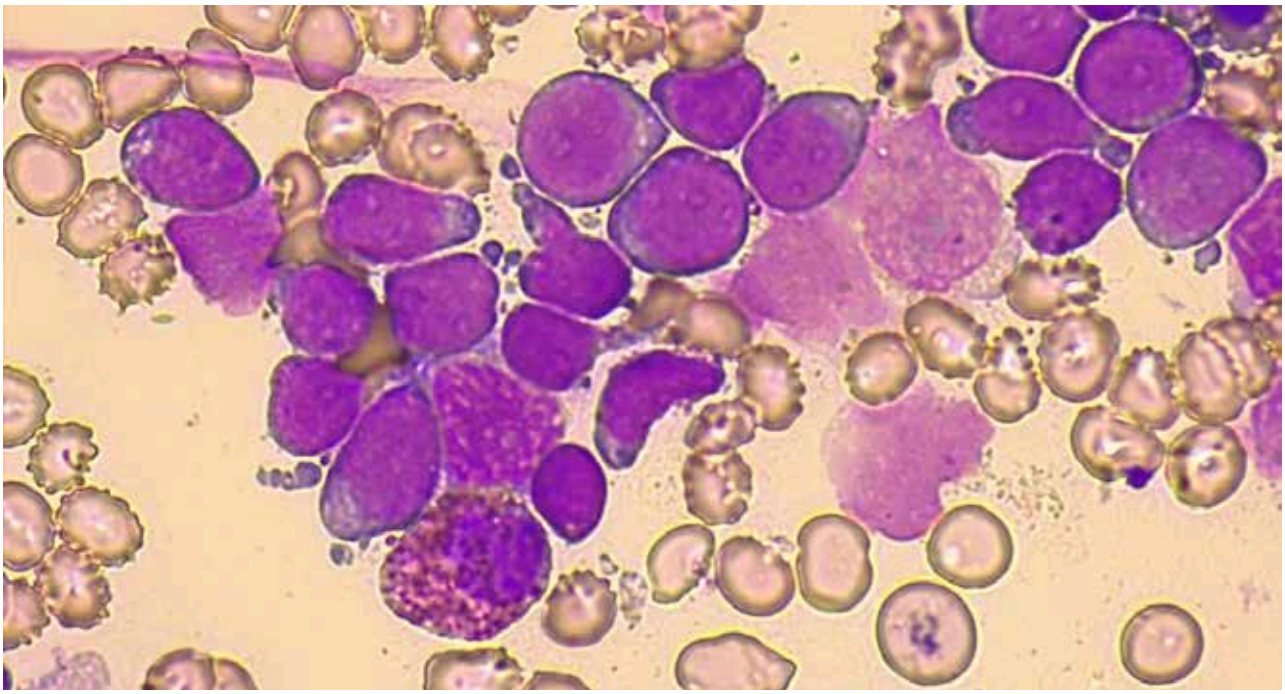
specific *in situ* sequencing (BaSISS) approach to map mutations in breast cancer tissue sections in a highly multiplexed manner, allowing, for the first time, spatial lineage tracing of cancer cell clones in the histological context, with Strell being a key member of this team (Lomakin et al., *Nature* 2022). The affiliation with CCBIO will enable Strell to adapt the *in situ* sequencing approach to the Hyperion mass imaging system for simultaneous mapping of genetic alterations and protein based cell typing. Also, Strell is working to decipher the immune architecture in DCIS; data on tumor infiltrating lymphocytes might define low risk DCIS (Schiza et al., *Eur J Cancer* 2022; Strell et al., *Clin Cancer Res* 2021). Strell recently received a pioneer grant from The Norwegian Cancer Society.

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. Further genetic and imaging mass cytometric (IMC) profiling is ongoing. So far, studies on estrogen related signaling networks and transcriptomic profiles have revealed an age-related gene expression signature tightly linked to proliferation and prognosis (Ingebriktsen et al., *Br J Cancer* 2022). Another study has shown a relationship between reduced GATA3 expression and poor patient survival (Sæle et al., in preparation).

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 **Bjørge group** is engaged in 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 2021-22, Bjørge and colleagues reported on spatial profiling and phenotypic characteristics of the microenvironment in ovarian cancers (Anandan et al., *Cancers* 2021). Data on immune profiling in ovarian cancer xenograft models after anti-PD-1 therapy has been presented (Kleinmanns et al., *Cancers* 2022). In a collaboration study, Bjørge and colleagues have presented data on the DNA methylome of cervical cells and risk of ovarian cancer (Barrett et al., *Nat Commun* 2022). Bjørge is currently president for NSGO (Nordic Society of Gynaecological Society), she is a faculty member for gynecologic oncology at ESMO and the leader of Oncology Forum (Norway). From November 2022, Bjørge is the Co-Director of CCBIO.





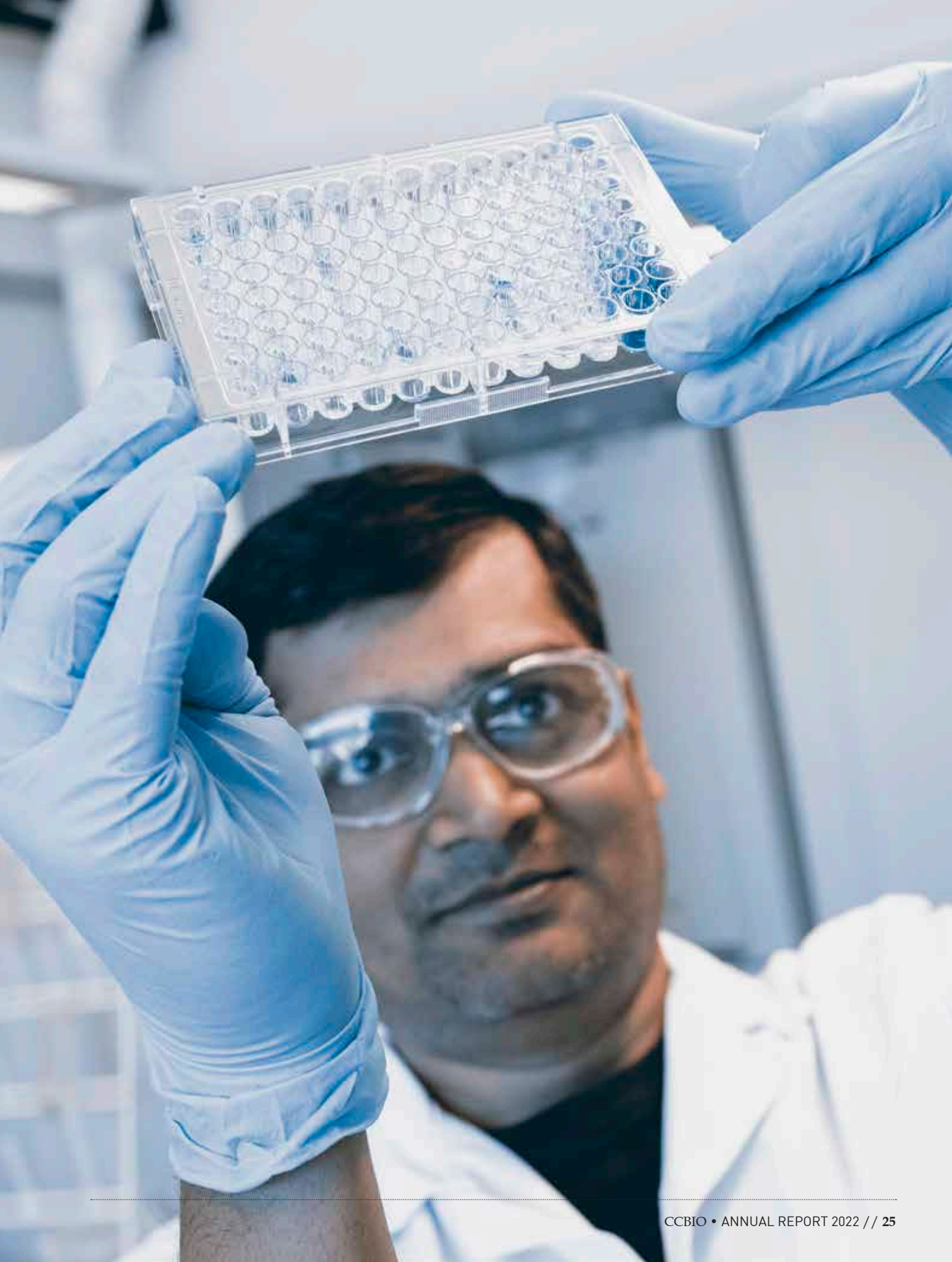
The **Gjertsen group** focuses on how intracellular signal transduction can be decoded to tell responders from non-responders early during cancer therapy. The experimental framework is based on tumor cells collected in clinical trials, dissecting how signaling in tumor cells is related to therapy response. In a recent key paper, Tislevoll et al. reported on early response evaluation by single cell signaling profiling in acute myeloid leukemia (*Nat Commun* 2023). In this study, it was reported that mass cytometry can be a valuable tool for early response evaluation and elucidate the potential of functional signaling profiling in precision oncology diagnostics. Further, Gjertsen is involved in multiple network projects. Huuhtanen et al. is the first to demonstrate a biological rationale for combining a small molecule inhibitor of ABL1 with immune therapy interferon alpha in a clinical trial (*J Clin Invest* 2022). Malani et al. follows up on a 2013 publication on *ex vivo* drug sensitivity screening in therapy guidance of the aggressive blood cancer AML. Notably, it is reported that as much as 60% of relapsed refractory patients can obtain therapy response if guided by drug sensitivity screen and gene expression analysis (*Cancer Disc* 2022). Also, Othman et al. indicate the complexity of AML genetics and how mutational panels are needed to optimize prognostication in AML (*Blood* 2022).

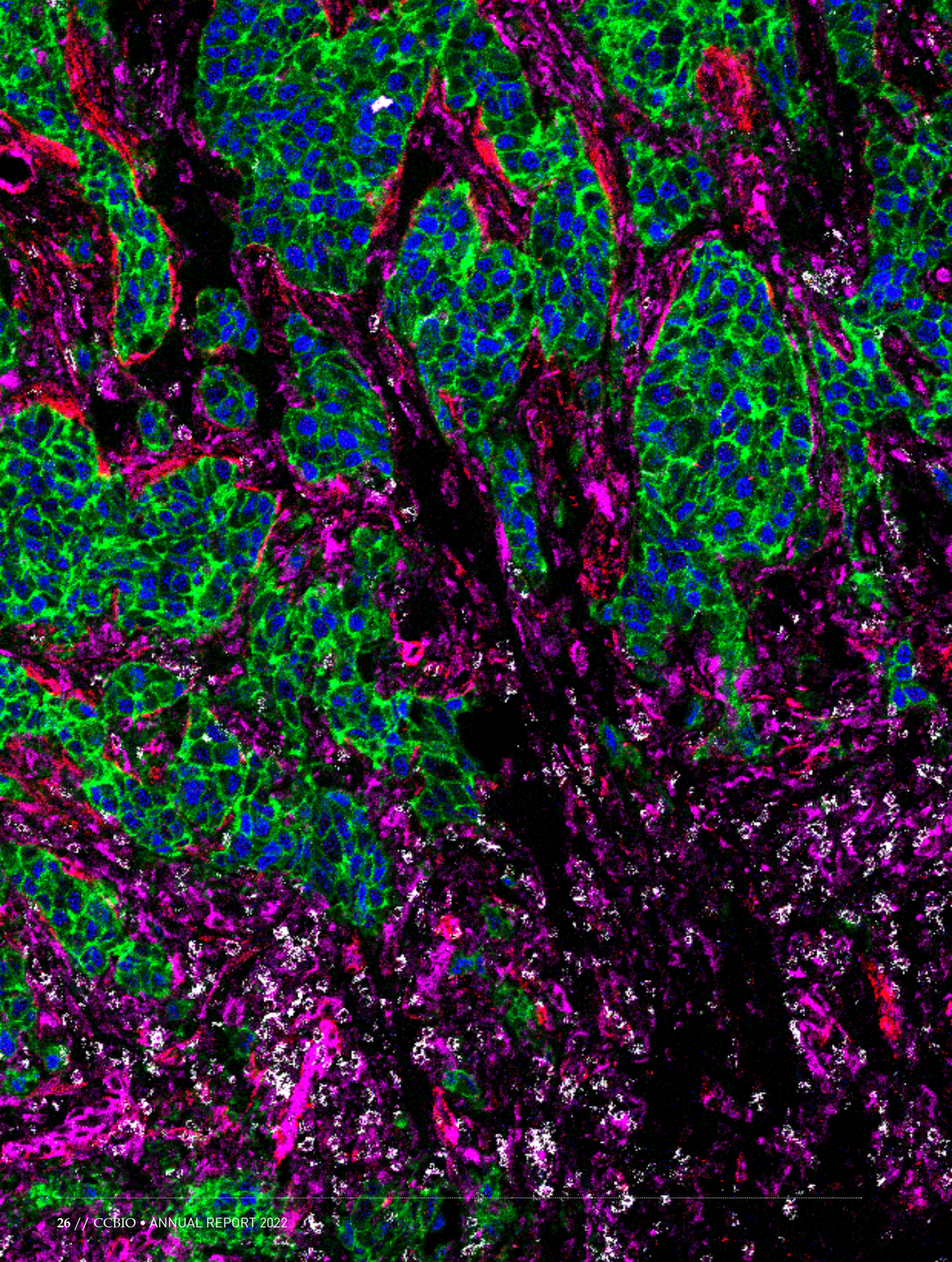
The **Straume group** is focusing on tissue biomarker studies in clinical trials. The group has reported an association between surgical tissue trauma and recurrence dynamics in high-risk breast cancer patients. A national academic trial combining anti-Axl treatment with immunotherapy is now closed (n=80) and is currently explored for treatment predictive markers of anti-Axl therapy in advanced melanoma cases. A national interventional study of patients with aggressive melanoma (IPI4; ipilimumab) is being analyzed, and some results have been presented. In 2021, data on ipilimumab treatment in metastatic melanoma from a phase IV trial was presented (Aamdal et al., *Int J Cancer* 2022; Aamdal et al., *ESMO Open* 2022).

In **TEAM 4**, the projects on ethics and economics of biomarker-based therapy are expanding and integrated in clinical trials. As CCBIO performs research on cancer biomarkers along the entire chain from studies of biological mechanism to clinical projects, the main societal impact resides in this sense in the improvement of cancer diagnostics and therapies and in medical innovation. The main measure of this impact is ultimately its effect on the quality and cost-effectiveness of cancer management, whereas it cannot be precisely measured in the short-term. Better knowledge of cancer biomarkers is likely to affect the prioritization dilemmas, although the nature of that effect depends on the nature of the knowledge to be discovered.

CCBIO integrates work on societal perspectives and has established a team structure led by **Strand** to improve interdisciplinary humanities and social science programs to study the opportunities and challenges of precision cancer medicine. The team will continue their collaborations on the more conceptual research into RRI and the coproduction of science, technology, and society.

A key insight in Team 4 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 between the **Strand group** and 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 **Strand group** performs research on the ethical, legal, and societal aspects (ELSA) of CCBIO's research, distinguishing between three 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); 3: A better understanding of complexity in cancer as illness, disease and sickness. The ELSA group of CCBIO interacts with and is 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. In 2022, the group reached an important milestone by the publication of the interdisciplinary research anthology *"Precision Oncology and Cancer Biomarkers: Issues at Stake and Matters of Concern"*, edited by Anne Blanchard and Roger Strand (Springer 2022). It constitutes a state-of-the-art volume on interdisciplinary research on goal 1 above and represents if not the final word from CCBIO on these issues, at least the major milestone. While research with a strong philosophical dimension rarely can be summarized in terms of "findings", we may say that the volume offers a range of suggestions for how to *reframe cancer* and how to resolve the various ethical and social dilemmas around cancer biomarkers and personalized/precision cancer medicine, including those of equity and social justice as well as challenges of excessive medicalization. The aspect of media debates has been further pursued in 2022, also suggesting reframing as the solution (Nilsen et al., *Norsk Medietidsskrift* 2022; Stenmarck et al., *BMC Med Ethics* 2022). In the first results from the collaboration with Bjørge's group (Gissum et al., *Cancer Care Research* 2022), the team shows how aspects of ovarian cancer as illness, are poorly represented in treatment of the corresponding disease. The results have direct clinical relevance.

The main idea for the following years is to deepen existing collaborations, including with Bjørge's group, and with Akslen and Bertolaso on the understanding of complexity in cancer, also along the lines of the Strand and Chu chapter *Crossing the Styx: If Precision Medicine Were to Become Exact Science* in the book *Precision Oncology and Cancer Biomarkers*, 2022, as well as to develop a stronger interdisciplinary collaboration with Cairns and Jiyeon Kang on the economic aspects of cancer biomarkers.

In the **Cairns group**, health economics research within CCBIO has focused on the economic evaluation of oncology drugs. Particular attention has been paid to the evaluation methods used and the contribution of different types of data (such as health outcomes recorded in clinical trials and real-world data). The most important project in recent years has been Jiyeon Kang's PhD project *Improving economic evaluation and decision-making for oncology drugs using real-world data*. This has involved a detailed analysis of two hundred and twenty-nine appraisals undertaken 2011-2021 (UK). Another project has focused on how molecular targeted therapies and immune checkpoint inhibitors for the treatment of non-small cell lung cancer have been assessed.

Managed Access Agreements are being used increasingly in the UK as a means of improving access to treatments where the evidence of clinical effectiveness is too uncertain for the National Institute of Health and Care Excellence (NICE) to recommend routine commissioning. The Cancer Drugs Fund [CDF] was introduced in England in 2016 to give patients access to these potentially valuable treatments. The CDF provides the drugs for several years while additional data are collected before a final review of the drug takes place. An analysis by the Cairns group of the first twenty-four drugs to exit the CDF, highlighted the important role played by longer follow-up of patients in the original clinical trials used to support the introduction of these drugs and the very limited role played by the data collected from patients receiving the drugs provided through the CDF. This is an important finding given the widespread enthusiasm for using real-world data to inform drug reimbursement decisions. Clear differences were observed between the appraisal of checkpoint inhibitors and that of molecular targeted therapies, at least in the context of non-small cell cancers. These differences derive from the more limited clinical data and the more restricted application of targeted medicines. In 2022, results were reported on the use of real-world data in access agreements appraisals of targeted cancer therapy (UK) (Kang et al., *Pharmacoeconomics Open* 2022; Kang et al., *BMC Cancer* 2022). Notably, Jiyeon Kang successfully completed her CCBIO funded PhD thesis in 2022 (at LSHTM).

In the **Norheim group**, the main aim has been to explore how biomarkers inform and potentially improve fairness in health care priority setting. Eirik Joakim Tranvåg's PhD thesis *(Precision and Uncertainty)* has been the main delivery. Findings in a conjoint analysis based on a survey of Norwegian medical oncologists suggest that biomarkers may be seen as relevant in clinical priority setting decisions for new and expensive cancer drugs. Results from an analysis of Norwegian drug appraisals also suggest that biomarkers are actively used and help facilitate drug coverage decisions at a national level. Despite this, Tranvåg argues in his thesis that priority setting actors still need to acknowledge that the increasing uncertainty in personalized medicine may lead to more difficult priority setting decisions. This cannot be dealt with only by developing better and more valid biomarkers, but also requires interaction between science and society, co-production of knowledge and a fair priority setting process.

Key publications from Norheim's group were Tranvåg's PhD thesis *Precision and Uncertainty: Cancer biomarkers and new perspectives on fairness in priority setting*, and the third and final paper in the thesis, *Appraising Drugs Based on Cost-effectiveness and Severity of Disease in Norwegian Drug Coverage Decisions* (published in *JAMA Network Open*, June 2022). The findings

from this paper must be seen as a major result from the group, as it was highly relevant for the public debate about drug reimbursement in Norway. The group contributed to both of CCBIO's anthologies on the ethical, legal and societal aspects of cancer biomarkers, the last issue being *Precision Oncology and Cancer Biomarkers, Issues at Stake and Matters of Concern* (editors Anne Blanchard and Roger Strand, Springer 2022).

During 2019-2022, 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. Notably, in 2022, Norheim was awarded a *Centre of Excellence (SFF)* from the Research Council of Norway.

The **Jonassen group** performs research in developing computational methods for analyzing and discovering patterns in molecular biology data. Since the 1990s, the group has worked with a variety of different data types; new technologies have become available and new application areas have developed. In the context of CCBIO, the work has naturally focused on development of methods relevant for cancer studies and in particular to understand tumor microenvironments focusing on the use of RNA-seq gene expression data and later single-cell CYTOF and imaging mass cytometry (Hyperion) data. Within the frames of CCBIO, the group has had access to groups with leading expertise in different cancer types and the possibility to take part in experimental design of new studies coupled with planning the computational analysis of the resulting data and possible follow-up experiments.

An important sub-project has been the AML_PM project which has been funded by ERA_PerMed including Gjertsen from CCBIO and a consortium including groups from Germany, the Netherlands and Canada. In this project, the team has combined systems biology modeling of targeted signaling systems with machine learning approaches aiming to help select treatment options for individual patients based on the status of signaling pathways. Another important sub-project has been the application of the Hyperion instrument to explore spatial aspects of tumor microenvironments of breast cancer. The team has studied alternative workflows for image data processing and graph representations of the extracted data. This will indicate interactions between different cell types and their states and link this with patient prognosis and treatment response – and develop new biomarkers and information guiding design of new therapies.

In conclusion, a range of research projects along with science education and communication have been conducted and reported on continuously since 2013. In addition, multiple new research initiatives have been conceived, in part based on increasing intramural collaboration and international networking. In addition to an increasing number of high-impact publications and four books presented by CCBIO (two of them published in 2022), multiple activities are being performed by the CCBIO Research School for Cancer Studies, with 12 core courses. Notably, the CCBIO Masterclass Program is now in its second year (2022-2023), with teaching and training of young investigators aiming for independency and future positions as group leaders. The CCBIO-ARC (advanced research colloquium) has been initiated. Notably, in 2022, Norheim was awarded a Centre of Excellence (SFF) from the Research Council of Norway. When CCBIO is now approaching the transition phase to CCBIO 2.0 and post-RCN continuation of the center, we plan ahead as we optimistically reflect on the "core concepts" and integrated activities of CCBIO and the strive for responsible real-life impact. ••

Scientific and Societal Impact

CCBIO's EVALUATIVE SELF-INQUIRY

Text: Roger Strand & Lars A. Akslen, CCBIO

2023 is the final year of the Centre of Excellence (CoE) grant awarded to CCBIO from the Research Council of Norway. The centre will continue and deliver cutting edge research, with a modified set-up. In 2022, CCBIO has begun its process of evaluative self-inquiry (de Rijcke et al., 2019; Völker et al., 2023) as a first step in the process of transformation and further improvements. As explained in previous annual reports, our methodological approach is to document not only high-visibility "extraordinary" impact but also what has been called "normal impact", the type of advancements that do not attract newspaper headlines but make up most of the scientific and practical progress in the real world (Sivertsen & Meijer, 2018).

During the autumn of 2022, the Centre Director Lars A. Akslen conducted conversations with all principal investigators with the aim of an evaluative self-inquiry, supported by Roger Strand. Initial impressions and results were then presented and discussed in a plenary seminar for principal investigators. While a lot of work remains, including the review process together with the Scientific Advisory Board, some preliminary topics for possible reflections and lessons have been identified. Among elements that often were highlighted in the conversations so far, we find the unusual breadth and scope of the CCBIO Research School, the added value of our international faculty, and the consolidation of the CCBIO symposia as a vital meeting place for cancer biomarker research of national and international importance. Another important element is how the CCBIO leadership has facilitated new scientific collaborations within and around the centre, not the least by strategic design and use of funding mechanisms. For our final report, we will dive deeper into the impact created in this way.

Finally, we are contemplating the lessons to be learnt on the scope of the research conducted in the centre. As expected, the research focus has become sharper over the years as the centre has developed and matured. Still, an important part of the identity of CCBIO has been to maintain considerable diversity, both in terms of the whole chain of translational research from basic and preclinical to clinical studies and trials, and in terms of the multi- and interdisciplinarity that also reached into the social sciences and the humanities.

Evaluative self-inquiries can of course never conclude objectively on the actual impact of a research endeavour. Neither are they instruments for self-praise. The purpose of the exercise is to identify achievements and lessons from our first decade as a CoE but also to identify strengths, opportunities and areas for improvement for our next stage as an excellent research environment. It is to take a breath and a moment to reflect before entering the next race. In this way, CCBIO has committed to produce a final report that perhaps also may inspire future CoEs and attract a readership beyond what is expected for the genre. ••

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RESEARCH PROGRAMS AND TEAMS

For the second term (2018-2023), the organization of CCBIO was modified to reflect the ongoing 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 with projects on ethics, economics, philosophy, and priorities (**TEAM 4**).

These four programs are supported by resources in bioinformatics and processing of big data, coordinated by Inge Jonassen, and Rolf Reed as a strategic advisor. Increased connectivity and collaboration within CCBIO have taken place over the years. The center is supported by an International Faculty of 14 top scientists in different fields.

T1

TEAM 1

MECHANISMS OF TUMOR MICROENVIRONMENT INTERACTIONS

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


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T1

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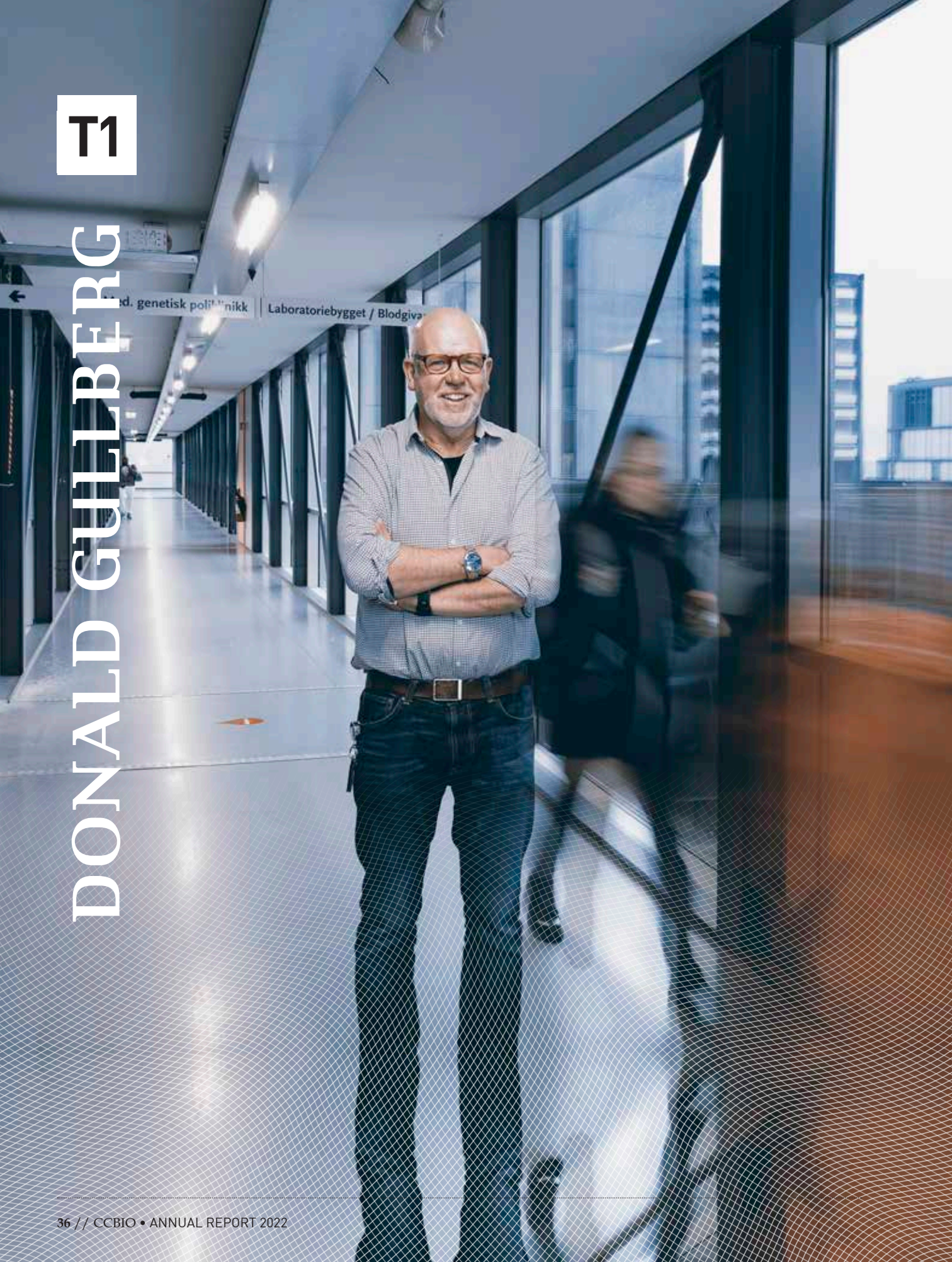


Research Focus
The research in the Gullberg group is focused on work related to integrin α11. The CCBIO projects deal with understanding the role of integrin α11 at the molecular and cellular levels in order to ultimately reach a better understanding of its role in the tumor stroma.

Subprojects
1. In one project, the group has developed a new fibroblast specific transgenic mouse strain where Cre-recombinase is driven by a human integrin α11 promoter (ITGA11-Cre strain). The first study presenting this novel mouse strain was published in 2020 in Matrix Biology Plus (Alam J. et al., Matrix Biol. Plus, 2020). The Cre mouse strain has now been bred with a tdTomato strain for direct visualization of ITGA11 expression.

2. A second project relates to the role of integrin α11 in skin squamous cell carcinoma (SCC), performed in collaboration with Ritva Heljasvaara from the University of Oulu. Focus is on the role of dermal stroma in a mouse model of SCC using the mouse strain deficient in integrin α11. The first results were published in 2022.

3. A third project relates to epitope mapping of integrin α11 mAbs. The group has finished epitope mapping of mAb 210F4 and is in the final stages of mapping epitopes of the function blocking antibody 203E1. This project is supported by a PhD student financed by the Medical Faculty and a NCS supported researcher, Cédric Zeltz, who started in 2022.

Important results
Establishing the ITGA11-Cre mouse strain was a major milestone in the group's work after 10 years of focused efforts on this project. The further breeding into a fluorescent reporter strain will be another step forward. The detailed epitope mapping of mAb 210F4 and mAb 203E1 to a few amino acids also illustrates the importance of consistent work spanning several years to reach long-lasting and well-cited results.

Future plans
The overall goal is to continue characterization of integrin α11 to evaluate its potential as a therapeutic target in fibrotic conditions including the tumor stroma. In specific:

1. In collaboration with Ritva Heljasvaara, the group has crossed the ITGA11-Cre mouse strain with a double-fluorescent strain enabling direct visualization of the dynamic α11 expression in tissues and tumor stroma without fixation or other treatments. A set of detailed experiments are now planned to characterize the cells derived from this mouse strain.

2. For the function blocking α11 mAb 203E1 antibody, the group continues to characterize the epitope profile although they have mapped epitopes to a few amino acids in a loop structure of the calf-2 domain. Since the antibody has been sequenced, the group would like to humanize it, and resources will be applied for. On a collaborative basis, crystallization of the Fab fragments of mAb 203E1 with recombinant α11β1 will be performed.

CCBIO significance
The group finds that CCBIO and its support has been very important through these 10 years, including running costs for experiments, technical support, affiliation of Ritva Heljasvaara, and a 3-year PhD position financed directly by CCBIO. Gullberg has enjoyed inviting and interacting with speakers at the CCBIO seminars and CCBIO annual symposia. ••

GROUP MEMBERS:

Gullberg, Donald: PhD, professor, group leader
Kusche-Gullberg, Marion: PhD, professor
Grigorian, Andre: master student
Grønning, Mona: chief engineer
Lu, Ning: PhD, senior engineer
Mato, Raúl Pérez: MS, PhD candidate
Musiime, Moses: PhD, postdoc
Rausch, Jana Maria: ERASMUS master student
Zeltz, Cedric: PhD, researcher

T1

KARL-HENNING KALLAND

Research focus
The main priority of the Kalland group is dendritic cell-based cryoimmunotherapy (CryoIT) as a new cancer treatment modality, including integrated drug discovery and biomarker development.

Subprojects
1. CryoIT: Having completed the phase I clinical trial for metastatic prostate cancer, the group now prepares for the next phase clinical trial. The main efforts in 2022 and forwards are directed towards robust production of potent therapeutic dendritic cells (DCs) in Bergen.

2. Drug Discovery and Biomarker 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), b-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 (cDC1) and type 2 (cDC2) that 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, then 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.

Drug Discovery and Biomarker Development: The group's repurposing strategy has previously published two compounds that inhibit β-catenin signaling in cancer cell lines, and the molecular targets and mechanisms were identified. Novel compounds with STAT3-inhibiting activity have been discovered, and one of the compounds exhibited dual inhibition of both androgen receptor (AR) and STAT3. Patent applications have been submitted. In parallel, relevant biomarkers are explored, e.g., T-cell receptor sequencing.

Future plans
The overarching focus and aim will be to develop enhanced immunotherapy against cancer. Kalland envisages a next stage clinical BASKET trial during 2023-2025 and a next generation CryoIT protocol thereafter. The BASKET trial will include patients with prostate cancer, kidney cancer and vulvar cancer. The next generation CryoIT protocol will be enhanced by more robust and potent therapeutic dendritic cells. Biomarker development and implementation in the next clinical trial includes T-cell receptor sequencing and *in vivo*-mimicking *ex vivo* culture models to assess lymphocyte and dendritic cell functionalities.

CCBIO significance
CCBIO has provided a platform and a supporting environment that has clearly catalyzed and promoted scientific interactions and development of ideas and projects. Both national and international interactions have been enhanced. Importantly, CCBIO has been a crucial forum for recruitment, motivation, and education of the next generation of scientists in cancer research. ••

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


EMMET MCCORMACK

Research focus
The main motivation of the PreCOS group is the development and effective translation of novel therapies and imaging strategies for the treatment of cancer, particularly cancers with limited therapeutic options.

Subprojects
1. Engaging IPSC techniques; the Norwegian Cancer Society funded project AMIDE will generate models of patient's disease, including the patients' own immune system for the ultimate personalized immuno-oncology models.

2. IDDEA funding from the Norwegian Cancer Society and in collaboration with OUS (Sébastien Wälchli) will evaluate novel CAR-T in ovarian cancers, with generation and implementation of innovative CAR T cell designs to increase tumor targeting specificity, safety and overcome T-cell exhaustion in the tumor microenvironment.

3. UiB Idé currently funds 2 concepts; In the first, the group will develop a novel dual CAR-T approach for the treatment of hematological malignancies, whilst the second will initiate the application of fluorescence image guided surgery in companion animals as a surrogate model to surgical intervention in the clinic.

4. The CoDaFlight project is centered around the development of time-domain fluorescence image guided surgery, funded by the EIC pathfinder program. The group will lead a work package evaluating this innovative concept in both mice and canine companion animals.

5. PARIS is an ERA-PerMED grant awarded to evaluate novel therapies and combination therapies in resistant ovarian cancer patients. The PreCOS group will develop models of resistance and evaluate therapies.

6. INTERCEPT-MDS is a MCSA-ITN action, from which PreCOS will host one ESR focused on the development of novel xenograft models of myelodysplastic syndromes (collaboration with Astrid Olsnes Kittang).

7. PERMIT, a H2020-funded project, will develop recommendations for robust and reproducible personalized medicine research. PreCOS involvement has been through work package 5 of this initiative where in collaboration with EATRIS, the group examined the role of preclinical modeling in academic and industrial development of personalized medicine.

8. Two projects are funded through the Norwegian Childhood Cancer Society; PICCA2 and PERCAP, which will both explore personalized medicine approaches to children's cancers (with collaborators Lars Herfindal, Sébastien Wälchli and Maria Winther Gunnes).

Important results
In a 2022 report, the group's intrabursal orthotopic PDX model of ovarian cancer – critical to the development of personalized therapies in this disease – was described in detail (Popa et al., Methods Mol Biol, 2022). Kleinmanns et al. (Cancers, 2022) further evolved this model to describe, for the first time, the development and application of a humanized orthotopic patient derived xenograft model of high-grade serous ovarian cancer. In this work, Kleinmanns described the parameters necessary to develop such a model, extensive functional analysis of humanization with CyTOF (34 markers) and application with anti-PD-1 inhibition. In the PERMIT project (described above), the group surveyed the use of preclinical modeling systems within academia and industry (Fosse et al., J Pers. Med, 2022). Subsequently, Fosse leads a team of internationally recognized scientists to establish recommendations of a framework for robust and reproducible preclinical research in personalized medicine (Fosse et al., BMC Med, 2023).

Future plans
Building on the results above and new collaborations with OUS, the group has several biomarkers under development as novel targets for CAR-T, which will be developed in their novel immunocompetent PDX models.

CCBIO significance
The group finds that several opportunities have opened through the CCBIO affiliation. Recent funding from NFR, NCS and EU is only possible based on the results from CCBIO funded projects. The collaboration with Line Bjørge, fostered during the term of CCBIO, has proven very synergistic, leading to long-term strategic planning and project funding, creating a wealth of opportunities. ••

GROUP MEMBERS:

Senior staff:
McCormack, Emmet: PhD, professor, group leader
Gelebart, Pascal: PhD, researcher
Popa, Mihaela Lucia: DVM, veterinarian
Wogsland, Cara Ellen: PhD, senior researcher

Junior staff:
de Montlaur, Constance de Villardi: PhD, researcher
Leitch, Calum: MS, researcher

Technical staff:
Fandalyuk, Zinayida: MS, staff engineer, lab manager
Benjaminsen, Susanne: MS, staff engineer
Safont, Mireia Mayoral: staff engineer

Postdoctoral fellow:
Kleinmanns, Katrin: PhD

PhD candidates:
Dowling, Tara Helen: MS
Gjerde, Christiane Helgestad: MD
Fosse, Vibeke: DVM, veterinarian
Mesquita, Ângela: MS
Sand, Louise Bergsjø: MS
Tandaric, Luka: MS

Master student:
Lode, Martine Rott

T2

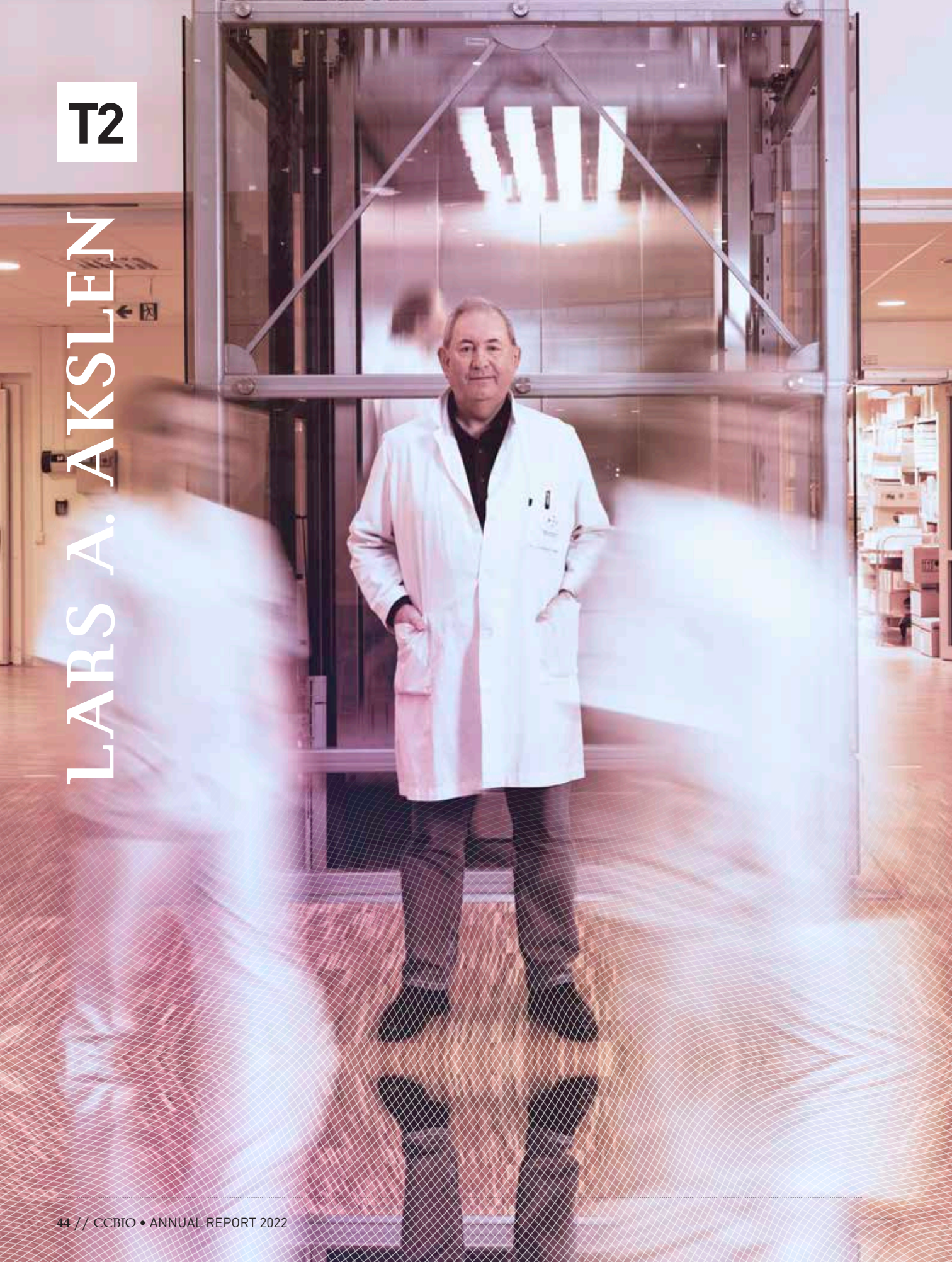
TEAM 2

DISCOVERY AND VALIDATION OF CANCER BIOMARKERS

The aim of this program is to explore and validate different classes of biomarkers in tissue and blood 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 predictive signals. This team consists of the Principal Investigators Akslen (CCBIO director) and Lorens, and the Associate Investigators Costea, Engelsen, Krakstad, Strell, and Wik.

T2

LARS A. AKSLEN



Research focus
The focus of the Akslen group has been to discover and validate novel tissue-based cancer biomarkers, especially related to the tumor microenvironment – for improved biological understanding and better prediction of aggressive tumor behavior and treatment response. The group concentrates on breast cancer proteomics (by Mass Spectrometry) and single-cell analytics by multi-marker spatial mapping of tumor tissues (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. Roles of Nestin and Stathmin in BRCA1-related and basal-like breast cancer

Important results
1. Proteomic profiling of laser capture micro-dissected breast cancer tissues has been performed, 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 (PAM50), also after external validation. For the first time, the group demonstrated 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).

2. Stromal protein profiles have been integrated with breast cancer cell line secretome data from baseline and hypoxic conditions, demonstrating metabolic reprogramming and differences between subtypes (Kjølle et al., in revision).

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

4. 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 (IMC) of Stathmin in association with immunogenic and angiogenic cell populations, searching for Stathmin related cellular niches as biomarkers and potential therapy targets (Askeland et al., in preparation). Nestin, which is associated with Stathmin in breast cancer, has been linked to aggressive phenotypes and stemness (Krüger et al., Sci Rep 2017). The role of Nestin in breast cancer is being explored by CRISPR-based knockdown and animal models (Ardawatia et al., in preparation).

In addition, Akslen has developed fruitful contact and collaboration with several members of the CCBIO International Faculty. In late 2022, a novel role of PRSS2 in the tumor microenvironment was presented in collaboration with the groups of Watnick and Brekken (Sui et al., Nat Commun; PMID: 36575174).

Future plans
The group will continue to use single-cell mapping of cancer architecture to define multicellular niches with potential functional importance. In particular, interactions between tumor cells and nerves, immune cells and vascular cells will be focused upon. Hopefully, this strategy will increase the precision of prognostic and treatment-predictive biomarkers. The group will further explore the phenotypic diversity and complexity of breast cancer subtypes.

CCBIO significance
As the CCBIO director since 2013, Akslen feels that it has been extremely rewarding to observe the increasing enthusiasm and motivation of all members and staff, with continuous developing and strengthening of joint projects and excellent achievements in education and mentoring. The support from international collaborators and advisors has been essential. For the Akslen group, the recruitment of young and energetic colleagues has been a key development in recent years, along with international contacts. ••

GROUP MEMBERS:

Researchers:
Akslen, Lars A.: MD, PhD, professor, group leader, CCBIO director
Arnes, Jarle B.: MD, PhD, associated researcher
Aziz, Sura, MD, PhD, associated researcher
Børretzen, Astrid: MD PhD, associated researcher
Carrasco, Manuel: PhD, researcher
Chen, Ying: MD PhD, associated researcher
Edelmann, Reidunn J.: MD, PhD, associate professor
Engelsen, Agnete S.T.: MS, PhD
Halvorsen, Ole Johan: MD, PhD, professor emeritus
Hugdahl, Emilia: MD, PhD, researcher
Kjølle, Silje: MS, PhD, researcher
Klingen, Tor Audun: MD, PhD, associated researcher
Knutsvik, Gøril: MD, PhD, associated researcher
Milosevic, Vladan: MD, PhD, researcher
Ramnefjell, Maria: MD, PhD, associate professor
Smeland, Hilde Ytre-Hauge: MD PhD, associated researcher
Stefansson, Ingunn M.: MD, PhD, professor
Wik, Elisabeth: MD, PhD, associate professor

Postdoctoral fellows:
Ehsani, Rezvan: PhD
Kleftogiannis, Dimitrios: PhD
Schuster, Cornelia: MD, PhD
Vethe, Heidrun: PhD

PhD candidates:
Askeland, Cecilie: MD
Bjørnstad, Ole Vidhammer: MS
Ingebriktsen, Lise M.: MS
Sæle, Anna Kristine Myrmel: MD

Pre-PhD projects:
Hugaas, Ulrikke: stud. med.
Tegnander, Amalie: stud. med.

Technicians:
Ardawatia, Vandana: PhD, senior engineer
Finne, Kenneth: PhD, senior engineer
Kalvenes, May Britt: PhD, senior engineer
Winge, Ingeborg: PhD, senior engineer

T2

JAMES LORENS

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

Subprojects and Important results
1. *AXL regulates DNA sensing and Type 1 interferon responses in tumors*: Aneuploid tumors are prone to activating the cytosolic DNA sensing pathway, comprising induction of type 1 interferons (IFN) with diverse effects on the innate and adaptive immune systems through antiviral effector molecules. Type 1 IFN responses in malignant cells or dendritic cells (DCs) are central mediators of response to immunotherapy.

The efficacy of chemotherapy harnesses the host immune response by inducing immunogenic tumor cell death and releasing adjuvant signals known as damage associated molecular patterns (DAMPs). AXL serves as an IFN-response checkpoint by blocking IFNAR1 and IFNAR2 signaling via suppression of cytokine signaling (SOCS1/3).

The group demonstrated that AXL kinase inhibition in combination with chemo-immunotherapy enhances type 1 IFN responses in different tumor immune contexts. The group provided the first evidence that AXL regulates type 1 IFN at the level of TLR activation in tumors, and AXL kinase inhibition enhanced type 1 IFN responses that correlated with increased infiltration of NK cells, CD4- and CD8-T cells into tumors. These results provide evidence that AXL inhibition leads to promotion of antitumor immune responses and better chemo-immunotherapy efficacy.

2. *AXL targeting restores PD-1 blockade sensitivity of STK11/LKB1 mutant NSCLC through expansion of TCF1+ CD8 T cells:* Mutations in STK11/LKB1 in non-small cell lung cancer (NSCLC) are associated with poor patient responses to immune checkpoint blockade (ICB). In mouse models, systemic inhibition of AXL resulted in increased type I IFN secretion from dendritic cells, restoring therapeutic response to PD-1 in tumors. NSCLC-affected individuals with identified STK11/LKB1 mutations receiving bemcentinib and pembrolizumab demonstrated objective clinical response to combination therapy. The conclusion is that AXL is a critical targetable driver of immune suppression in STK11/LKB1 mutant NSCLC.

Future plans
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 of the randomized phase II clinical trial (NCT02872259) to evaluate AXL targeting to improve immunotherapy efficacy in malignant melanoma.

CCBIO significance
CCBIO has significantly improved the group's research by facilitating collaborations with both local and international investigators, including improved training for students. The annual symposium has been particularly successful, creating a forum for scientific exchange. ••

GROUP MEMBERS:

Senior researchers:
Lorens, James: MS, PhD, professor, group leader
Bougnaud, Sebastien: MS, PhD, associated researcher
Engelsen, Agnete: MS, PhD, senior researcher
Røsland, Gro Vatne: MS, PhD, researcher

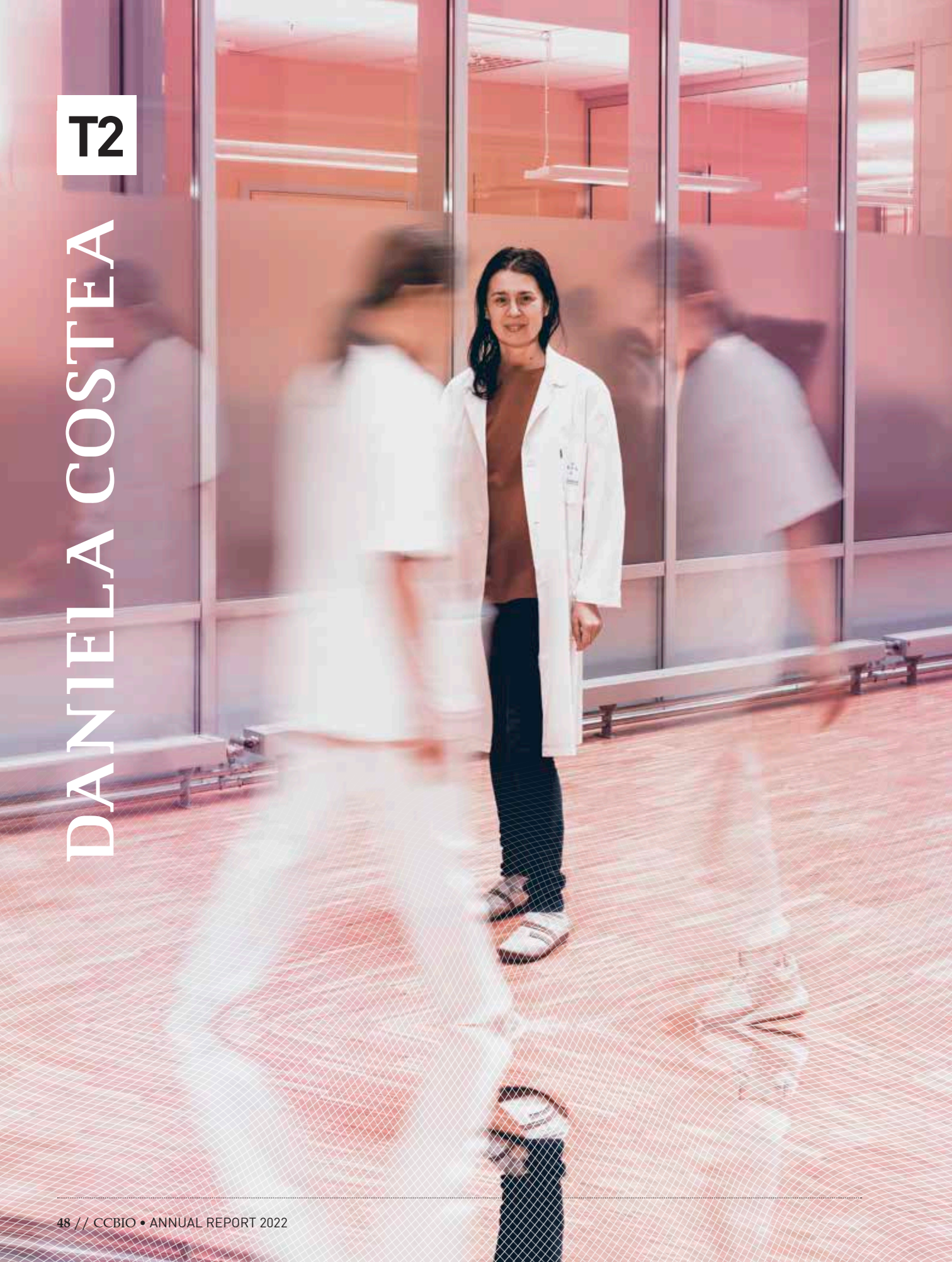
Postdoctoral fellows:
D'Mello, Stacey: PhD
Lotsberg, Maria Lie: PhD
Moutoussamy, Emmanuel Edouard: PhD

PhD candidates:
Dhakal, Sushil: MS
Grøndal, Sturla Magnus: MS
Rayford, Austin: MS
Siraji, Muntequa Ishtiaq: MS

Technicians:
Han, Jianhua: head engineer
Lu, Ning: senior engineer
Stigen, Endre: head engineer

T2

DANIELA COSTEA



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

Subprojects
1.Mechanisms of tumor-stroma (fibroblasts) interactions

2. Stroma as a source of prognostic biomarkers

3. Development of *in vitro* models as bio-tools for functional cancer diagnostic

Important results
The group has recently identified twelve differentially expressed miRs in stromal fibroblasts of head and neck cancer (HNC) lesions compared with normal oral mucosa (Rajthala et al., Int J Mol Sci, 2021), and miR-138 was one of them. The functional roles of miR-138 dysregulation in cancer associated fibroblasts (CAFs) from HNC have been studied. Ectopic miR-138 expression reduced fibroblasts' motility and collagen contraction ability and suppressed invasion of suprajacent HNC cells, while its inhibition resulted in the opposite. Transcript and protein examination after modulation of miR-138 expression showed changes in CAF phenotype-specific molecules, focal adhesion kinase axis, and TGFβ1 signaling pathway. The group's study showed that miR-138 in HNC-derived CAFs exhibits a tumor-suppressive function (Rajthala et al., Front Oncol, 2022).

The highest incidences of HNC are in Sub Saharan Africa and South-East Asia. Costea collaborates with many hospitals in these countries, among them in Sudan. In this study, the team evaluated patterns of immune cell infiltration at the invasive tumor front (ITF) in a prospective cohort of HNC patients attending Khartoum Dental Teaching Hospital. All inflammatory cell subsets investigated were found to be higher in the stromal compartment as compared to the epithelial one, except for the PD-L1+ subset. Stromal infiltration of CD8+ cells was associated with low tumor budding scores. The presence of PD-L1 was found to be associated with unfavorable overall survival, and Cox's analysis using an age- and tumor-stage-adjusted model, identified epithelial PD-L1 expression at the ITF as the only independent prognosticator (Gaafar NM et al., Clin Exp Dent Res, 2022).

In order to develop novel therapies for HNC targeted at "normalization" of the tumor-CAF interactions, the group performs studies focusing on the tumor-stroma interactions in normal oral mucosa. Using 3D organotypic models of normal oral mucosa developed from primary cells of healthy volunteers, they found that the fibroblast-derived growth factors GM-CSF and KGF are responsible for regulating major aspects of oral epithelial differentiation (Das et al., Eur J Oral Sci, 2022).

Future plans
The group is focusing on deep characterization of fibroblasts' heterogeneity and their interaction with various subpopulations of cancer cells and inflammatory and endothelial cells by use of imaging mass cytometry (the Hyperion platform). Based on IMC findings, a panel of biomarkers that characterizes different subsets of CAFs in HNC and vulva cancer (VC) will be established.

The group is also developing robust *in vitro* 3D tumor models for dissecting tumor-stroma interactions at the molecular level and for high throughput drug testing in HNC, VC and penile cancer (PC).

CCBIO significance
Costea finds that being part of CCBIO through the years has given her group access to an excellent research environment, given her students the opportunity and benefit of being part of the CCBIO Research School for Cancer Studies, and facilitated new and very fruitful collaborations. ••

GROUP MEMBERS:

Senior researchers:
Costea, Daniela Elena: DDS, PhD, professor, group leader
Dabija-Wolter, Gabriela: PhD, associate professor
Johannessen, Anne Christine: MD, DDS, PhD, professor
Neppelberg, Evelyn: DDS, PhD, associate professor
Suliman, Salwa: DDS, PhD, senior researcher

Postdoctoral fellows:
Dongre, Harsh: NanoMS, PhD
Parajuli, Himalaya: DDS, PhD

PhD candidates:
Baysal: **Eylem,** MS
Das, Ridhima: DDS
Dhakal, Sushma Pandey: DDS
Micongwe, Moses Isyagi: BDS, Mmed
Mohamed, Hassan Abdel Raouf-Ali: DDS
Mohamed, Nuha: DDS
Mustafa, Rammah: MS
Owibingire, Sira Stanslaus: MD
Rajthala, Saroj: MS
Tornaas, Stian: MS
Xenaki, Victoria: DDS

Pre-PhD projects:
Aljiafiri, Asia: master student
Debnath, Kala Chand: DDS, master student
Fjeldstad, Karoline: medical student
Kimo, Magnus: medical student
Siyam, Diana: dental student
Zaraq, Tariq Jan: master student

Guest researchers:
Alvarez Rivas, Carla: DDS, PhD
Litlekalsøy, Jorunn: MS, PhD
Mohamed, Nazar: DDS, PhD
Papyan, Robert: MD

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


T2
CAMILLA KRAKSTAD

Research focus
The Bergen Gynecologic Cancer Research Group focuses on molecular profiling of endometrial and cervical cancers, to better understand genetic 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. In recent years, a special focus has been on establishing patient-derived organoid model systems for endometrial cancer alongside continuous effort to gain knowledge of the genetic landscape.

Subprojects
In a large biomarker study of endometrial cancer, the group compared the mismatch repair (MMR) status between preoperative and operative samples. They also performed a large study to investigate the effect of treatment on patient-reported quality of life to gain insight into long-term consequences of treatment. For cervical cancer profiling, the team has been part of a multi-national consortium to unravel differences between cervical cancer cohorts from three continents. Within radiomics and radiogenomics, the group's competence has been combined to integrate genomic and radiology data for improved pre-operative diagnostics both for endometrial and cervical cancer patients.

Important results
In a study investigating MMR status in paired preoperative and operative endometrial cancer biopsies, the group demonstrated a substantial agreement in MMR status between paired lesions. They also found that in addition to determining MMR status, MMR protein expression levels, particularly MSH6, may add prognostic information in endometrial cancer. For cervical cancer, multi-omic analysis of 643 cervical squamous cell carcinomas identified two therapy-relevant subtypes that share the same defining characteristics across three geographically diverse cohorts. Among several projects on optimal integration of preoperative imaging, the group performed a study of the diagnostic performance of four different preoperative imaging workups for prediction of lymph node metastases (LNMs) in endometrial cancer. This work proposes a diagnostic workup with selective PET-CT in patients with high-risk MRI findings. In the group's quality of life study, patients with endometrial cancer receiving adjuvant chemotherapy reported significantly reduced functioning and more symptoms up to two years after treatment. For patients treated by surgery alone, surgical staging did not seem to affect the quality of life or symptoms to a measurable degree at follow-up.

Future plans
Two main projects on multiplex IMC (Hyperion) are ongoing, aiming to define markers for recurrent disease in low-stage endometrial tumors, and to define clusters of stem cells, also in endometrial cancers. The group will continue to develop their molecularly defined models for endometrial cancer and use these models for drug testing, functional experiments, and exploration of subtype specific genetic alterations. There is a close collaboration with colleagues at the Broad Institute and Dana Farber Cancer Institute, Harvard, Boston, to identify dependencies and drug-resistance in these models. The group will continue to have a strong focus on the MOMATEC2 trial and continue studies of radiomics and radiogenomics in uterine cancers.

CCBIO significance
CCBIO provides a platform for collaborations, discussions, and education between researchers with complementary interests and background. For the younger colleagues, the research school has been instrumental by inspiring and educating new talents and establishing networks. Available infrastructure has enabled new research projects and added new possibilities to explore biomarkers in cancer. ••

GROUP MEMBERS:

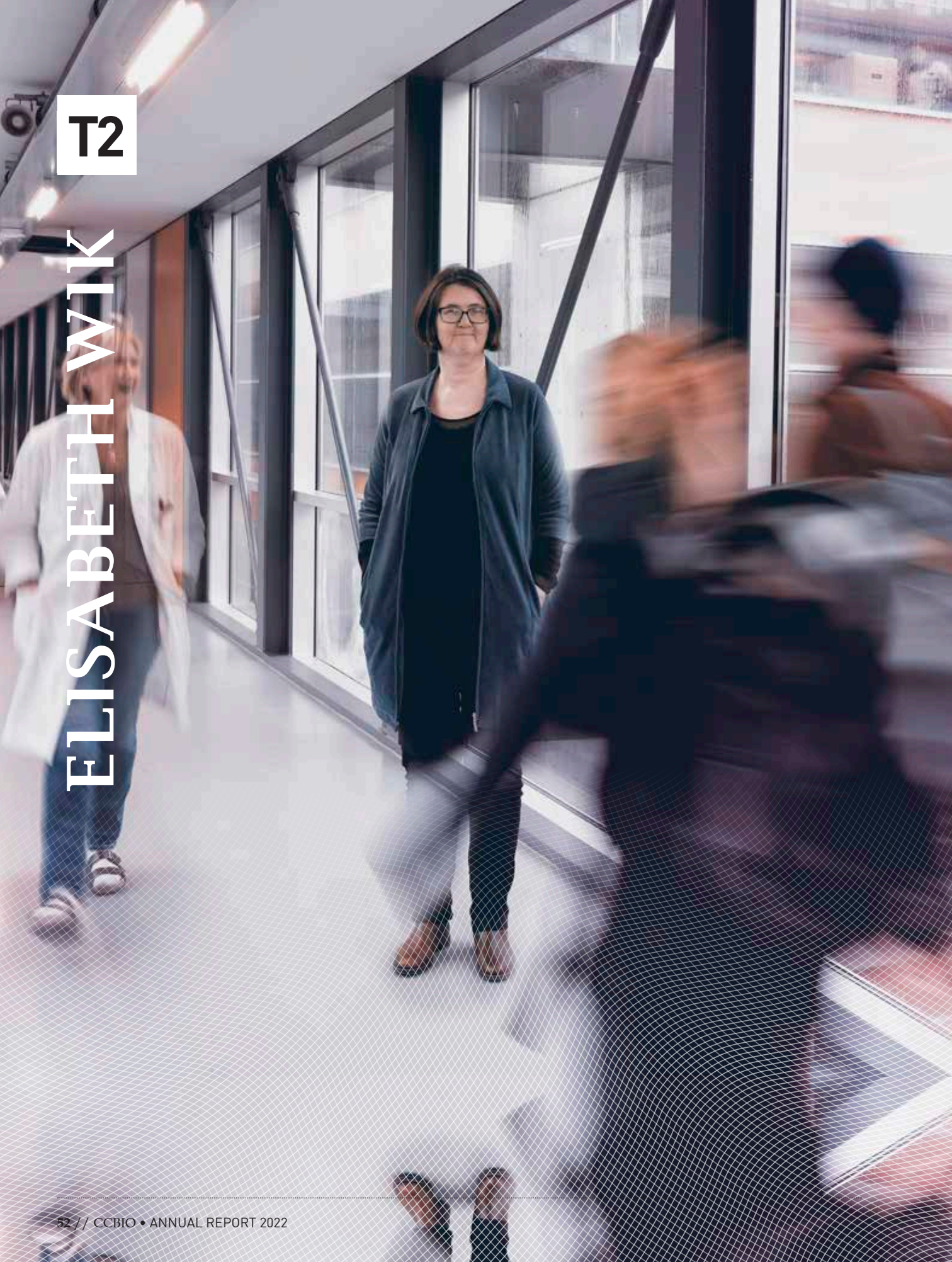
Senior researchers:
Krakstad, Camilla: professor, MS, PhD, group leader
Haldorsen, Ingfrid: MD, PhD, adjunct professor
Trovik, Jone: MD, PhD, professor

Postdoctoral fellows and researchers:
Berg, Hege Fredriksen: MSc, PhD, postdoc
Hodneland, Erlend: MS, PhD, associate professor
Espedal, Heidi: MS, PhD, postdoc
Gold, Rose Meng: researcher, computational scientist
Halle, Mari Kyllesø: MS, PhD, researcher
Høivik, Erling: MS, PhD, researcher

PhD candidates:
Dybvik, Julie: MD
Eldevik, Kristine Fasmer: MS
Gulati, Ankush: MD
Hjelmeland, Marta Espevold: MS
Kaliyugarasan, Satheshkuma: MS
Lien, Hilde: MS
Lura, Njål Gjerde: MD
Wagner-Larsen, Kari Strøno: MD
Åse, Hildegunn Siv: MS, MD

Clinical staff and technicians:
Bozickovic, Olivera: MS, PhD, staff engineer
Dugstad, Jenny Margrethe: MS
Enge, Elisabeth: study nurse
Flatekvål, Helene Midtun: MS, head engineer
Forsse, David: MD, PhD, consultant
Madissoo, Kadri: MS, head engineer

Medical Student Research Program students:
Bredin, Hanna
Eide, Agnes Jørgensen
Lyngstad, Jenny
Myrvold, Madeleine
Van den Berg, Madeleine: visiting student


T2
ELISABETH WIIK

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 – a project of high clinical relevance.

The patients being studied in BCY-B need clinical attention, and identifying patients that may be spared adjuvant treatment is of high importance. From the molecular analysis perspectives, integrating different levels of large-scale data has been a challenge in the omics studies and needs to be addressed in forthcoming BCY-B studies.

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 immune-angiogenic responses in breast cancer

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

Important results
The BCY-B group has established well-annotated, long-term follow-up cohorts of tissue from the BCY patients, including matched primary and metastatic tissue. One paper has been published (Ingebriktsen et al., BJC, 2022), and projects on GATA3, FOXA1, AGR2, and TFF1 are ongoing as part of the subproject "Estrogen receptor-related biology in breast cancer of the young" (Helse Vest funded in 2020). Studies of transcriptional age-dependent alterations and molecular subtypes in metastases from breast cancer of the young are in progress.

The BCY-B group is in early phases of studying genomic and epigenomic alterations in primary breast cancer and metastases – aiming for improved understanding of age-related variations in the metastatic processes. The group has since 2019 built a research group counting three PhD candidates, three Medical Research Program students (and one completed), one researcher, and one pre-PhD candidate.

Future plans
The BCY-B group aims to explore age-related biological differences, focusing on the metastatic processes. The group still aims part of their work towards biomarkers for response to endocrine therapy and plans to expand on genomic and epigenomic methods, integrating data from these with microenvironment markers under study. Further expansions of BCY cohorts, including tissue data, are ongoing. Efforts to attract external funding and establishing international collaborations and networks are planned.

CCBIO significance
Wik finds that being part of CCBIO has provided a motivating research environment, stimulating her to establish an independent research group. She finds the center to represent a vivid extended research environment for the students and candidates with vast possibilities for joining high-quality courses, seminars, and workshops, and providing all CCBIO members with valuable networking possibilities both locally and with international faculty. ••

GROUP MEMBERS:

Senior researchers:
Wik, Elisabeth: MD, PhD, associate professor, group leader
Høivik, Erling: PhD, researcher

PhD candidates:
Humlevik, Rasmus Olai Collett: MD
Ingebriktsen, Lise Martine: MS
Sæle, Anna Kristine Myrmel: MD

Medical student:
Syrtveit, Astrid

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

T2

CARINA STRELL

Research focus
The research in Strell's group focuses on the biology of breast ductal carcinoma *in situ* (DCIS), with the overall ambition to comprehensively elucidate the underlying regulatory signaling mechanisms of early breast cancer evolution towards clinical disease progression and therapy response. Special emphasis is placed on understanding the interplay between genetic alterations and the tumor microenvironment by using state-of-the-art spatial mapping techniques for tissue analysis. Strell's team further reaches beyond biological aspects and aims to uncover novel therapeutic opportunities as well as clinically relevant treatment stratification models for women with early breast cancer.

Only few DCIS lesions have the potential to progress to invasive breast cancer. However, since the regulatory mechanisms of cancer evolution are still largely undefined, a biological or clinical prediction of disease progression and therapy response remains difficult. The consequence is a high risk of over- as well as undertreatment for women with early breast cancer. Thus, improving guidance for clinicians and optimizing therapy applications is a major task for precision medicine.

Subprojects
1. EvoMaps – understanding the interplay of genetic alterations and the tumor microenvironment in DCIS

2. DCIS immune architecture

3. *ImSignal* – Mapping active immune cell signaling

Important results
EvoMaps: This project aims to adapt the *in situ* sequencing approach (Svedlund et al., EBioMedicine, 2019; Lomakin et al., Nature, 2022) to the Hyperion mass imaging system in order to enable a simultaneous mapping of genetic alterations and protein based cell typing and signaling pathway activation in diagnostic tissue sections. With this approach, the group hopes to be able to identify the regulatory mechanisms beyond subclonal expansion in DCIS and how they relate to tumor progression and the development of radioresistant traits.

DCIS immune architecture: The group has demonstrated that a high level of tumor infiltrating lymphocytes (TILs) in DCIS is associated with worse prognosis (Schiza et al., Eur J Cancer, 2022). During this work, distinct TILs patterns were noted (Thurfjell et al., in preparation). Using imaging mass cytometry, the project aims to uncover cellular subtypes and signaling pathways within these distinct TILs patterns and how they are linked to clinical outcome and radiotherapy response.

ImSignal: This is a new project inspired by previous work of the group where proximity ligation assay (PLA) based detection of PD1-PDL1 interactions was found to provide a more refined patient stratification than PD-L1 protein alone (Lindberg et al., in preparation). Aiming to gather better insights into the resistance mechanisms towards immunotherapy in breast cancer, the *ImSignal* project intends to perform a highly multiplex detection of active immune checkpoint interactions in tissue samples by adapting the PLA to the Hyperion mass imager.

Future plans
The research team will prioritize the adaptation of their established spatial tissue profiling techniques (*in situ* sequencing, PLA) to the Hyperion system. This will complement the ongoing spatial proteomics efforts at CCBIO with approaches for spatial genomics and signaling pathway mapping. The group will also seek contacts with CCBIO bioinformaticians and big data specialists to facilitate the integration of multiple layers with different spatial omics data into current bioinformatical analysis pipelines for deep tissue profiling.

CCBIO significance
Strell's group joined CCBIO in 2022. She finds that CCBIO offers a perfect environment, both with regards to the technical equipment and also the multidisciplinary competencies, to establish new methodological advancements for spatial tissue profiling and biomarker discovery. ••

GROUP MEMBERS:

Carina Strell recently received a Trond Mohn Foundation (TMS) Starting Grant starting July 1, 2022. The TMS Starting grants allow selected up and coming researchers to establish their groups with the later prospect of tenure track at the UiB. At the close of 2022, Strell was in the process of recruiting several new group members for her UiB-based group. In addition, Strell will retain her collaboration with Uppsala University (UU) through an adjunct position there.

Senior researcher:
Strell, Carina: PhD, TMS Starting Grant researcher at UIB, group leader

Postdoc:
Schiza, Aglaia: MD, PhD

PhD candidates:
Lindberg, Amanda: MS
Thurfjell, Viktoria: MD

Pre PhD candidate:
Hellberg, Louise

Lab manager:
Hekmati, Neda: (50%)

T2

AGNETE ENGELSEN

Research focus
The Engelsen group is dedicated to exploring how phenotypic plasticity interferes with therapeutic efficacy and immune cell-mediated killing. Through national and international collaborations, the group aims to unravel the best molecular targets to prevent phenotypic plasticity-driven therapy resistance and immune escape in solid tumors and to contribute to the design of better predictive tools for immune-oncology.

Subprojects
The group has recently established a local interdisciplinary collaboration that allows them to generate benign and non-small cell lung cancer (NSCLC) patient-derived organoids and explant cultures from lobectomy specimens (Hoareau et al., 2021, Ekanger et al., 2022), working on characterizing how well the models preserve the various NSCLC histological subtypes.

Hypoxia is a major driver of an aggressive and immune evasive tumor microenvironments (Zaarour et al., 2021, Engelsen et al., 2022). In one subproject, the group explores how hyperbaric oxygen therapy may be applied to improve the efficacy of immune checkpoint inhibition by modulating the metabolism of and the crosstalk between malignant cells and cells of the tumor immune microenvironment.

Important results
The group has shown how intrinsic differences in spatiotemporal organization and stromal cell interactions between isogenic lung cancer cells of epithelial and mesenchymal phenotypes can be revealed by high-dimensional single-cell analysis of heterotypic 3D spheroid models (Lotsberg et al., Front Oncol, 2022). This project serves as an important technical achievement for the group, and the study supports further applications of their complementary models in pre-clinical drug testing combined with high-dimensional single-cell analysis. This combination is expected to reveal cancer-stroma interactions and advance the understanding on the impact of epithelial phenotypic plasticity on innate and acquired therapy resistance in NSCLC.

Future plans
The NSCLC explant models recapitulate the complex tumor-immune microenvironment, and current projects aim to elucidate the effect of phenotypic plasticity on the spatial organization of the tumor immune microenvironment and explore how therapeutic targeting of phenotypic plasticity synergize with immune checkpoint inhibition (ICI) therapy, which serves to release the brakes that cancer cells can put on the immune system.

CCBIO significance
Engelsen appreciates the opportunity to collaborate with local and international CCBIO faculty, and the opportunity to participate in the Masterclass program. She also appreciates the opportunity to participate in organizing courses and activities related to the Research School for Cancer Studies (RSCS) and the INTPART-II research and educational collaboration. ••

GROUP MEMBERS:

Senior researcher:
Engelsen, Agnete S.T.: MS, PhD, group leader

PhD candidates:
Ekanger, Camilla T.: MS
Rayford, Austin J.: MS

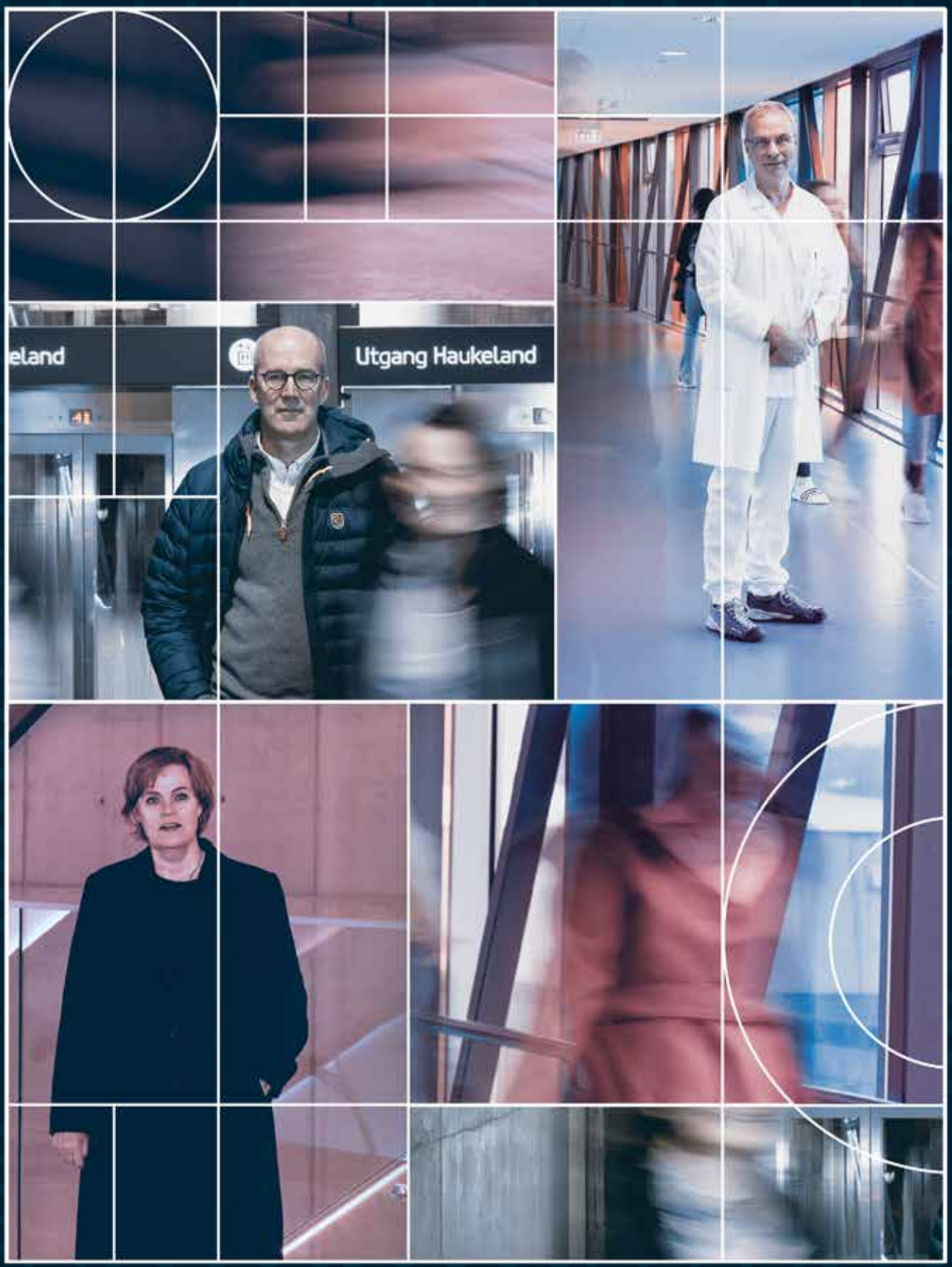
Master students:
Guttormsen, Maren Sofie F.
Arnal, Emmanuelle Lucie

T3

TEAM 3

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 (CCBIO co-director from November 16), Gjertsen (CCBIO co-director until November 16), and Straume.


eland
Utgang Haukeland

T3

LINE BJØRGE

Research focus
The aim of the group is to explore the pathogenesis of high-grade serous ovarian carcinoma (HGSOC), including the molecular (BRCA mutations, HR defects) and phenotypic (platinum sensitivity, degree of debulking) profiles and how these 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.

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

In order to accomplish the vision, Line Bjørge has together with Emmet McCormack set up a research team named INOvA (Innovative Novel Ovarian cancer treatment Approaches) that works with and focuses on the various programs. A team of extraordinarily skilled and motivated young researchers has been established, with a research environment that is in a unique position to combine tumor-profiling knowledge and preclinical modeling with implementation studies. The work focusing on how transitions is lost in translation in women living with ovarian cancer is conducted together with Roger Strand.

For vulva cancer, a rare disease where the stroma determines 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 have been established together with Daniela Costea and Karl-Henning Kalland.

Important results
The team has established tools for deep-tissue profiling, a mouse xenograft model platform, unique organoid platforms, near-infra-red (NIR) probes for tumor identification, and instruments to understand how it is to live with ovarian cancer as well as early-phase studies with modern design. These discoveries represent the foundation for ongoing and future projects.

The team's two-investigator initiated early-phase clinical studies are still open; the IMPACT-study has finish recruitment, while enrolment to the INFLUENCE-trial is still ongoing.

Future plans
Inherent tumor biological characteristics of HGSOC and vulva cancer influence the effect of different therapies (surgery, radiotherapy, chemotherapy, and targeted therapeutics), and to be able to select more individualized treatment establishment and validation of preclinical platforms for deep-tissue profiling, as well as drug screening, are necessary. Given the importance of surgery for both diseases, tumor targeted fluorescence-image guided surgery methodologies will be further developed.

Objectives:
1. To characterize the immunobiology of HGSOC and vulva cancer

2. To integrate the use of single-cell profiling of well-defined clinical trial cohorts to define biomarkers and preclinical models (organoids and 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 be able to present biomarker information to patients in a user-friendly way to avoid therapeutic misconception

CCBIO significance
Bjørge finds that the focus for the research projects fits well with the overall aim of CCBIO, and elements from all the four different main programs are included. Bjørge and McCormack belong to different teams, Teams I and III, respectively. Collaborative efforts have been set up with Costea (Team II), Kalland (Team I) and Strand (Team IV). She finds that the group's participation in CCBIO has resulted in establishment of new and fruitful collaborations and secured research funding (positions and running costs) as well as education and training. ••

GROUP MEMBERS:

Bjørge, Line: MD, PhD, MBA, professor, group leader
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

T3

BJØRN TORE GJERTSEN

Research focus
The signaling networks in cells are heavily dependent on a system of kinases and phosphatases, signaling enzymes that orchestrate regulation of cellular processes including cell proliferation and cell fate. The Gjertsen group focuses on how intracellular signal transduction can be decoded to early tell responders from non-responders in cancer therapy. The experimental framework is based on single cell profiling of tumor cells collected in clinical trials, dissecting how signaling in tumor cells is related to therapy response. The molecular pathway from cell surface by the receptor tyrosine kinase down to the transcription factor and tumor suppressor p53 is examined by mass cytometry, proteomics and gene expression analyses. The group is hypothesizing that the signaling pathway and the effector protein p53 can be viewed as integrators of information about proliferative activity and cellular fate. Therefore, decoding the signaling pathways and p53 may provide precise information about therapy response.

Signal transduction is directly involved in leukemogenesis of more than 50% of the aggressive blood cancer acute myeloid leukemia (AML). This is reflected in a spectrum of recurrent mutations found in the progenitor cells, including receptor tyrosine kinases like FLT3, RAS-genes, and tyrosine phosphatases. The Gjertsen group has chosen chronic myeloid leukemia (CML) for comparison to AML.

Subprojects
Subprojects include single cell immune and signal 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 ABL1 kinase inhibitors. However, the level of phosphorylated STAT3 indicate how effective the CML therapy is.

In AML, the group is examining whether signaling pathways from receptor tyrosine kinases, e.g., the MAP kinase pathway, may contain information about response to therapy and length of survival. Particularly, they examine whether the therapy given to the patients can be used as a stress test to enhance the predictive power of long-term response.

Preliminary data with the AXL inhibitor bemcentinib reflects this manifold genetic background of AML. The complexity of the tumor-host interaction indicate that these comparative analyses will take time.

The group's p53 research examines whether p53 isoform patterns are biomarkers of response. The wild type p53 protein reacts to most if not all cancer therapies. Ongoing work addresses how AXL may regulate the p53 protein and its isoforms. This may be an elegant link between the known function of p53 in cell differentiation and quiescence and the therapeutic effects of AXL inhibition.

Important results
Together with Nordic collaborators, the group has shown that kinase inhibitor therapy combined with interferon alpha broaden the immune repertoire in CML. For response prediction in AML, a combined gene expression profiling with *ex vivo* drug sensitivity screens are effective in more than 60% of the patients. This forms a foundation for future functional signaling analysis of single cancer cells.

Future plans
CCBIO version 2.0 could be a platform to evaluate the concept of early signaling response evaluation in solid cancers followed by adaptive treatment, e.g., by developing single cell techniques analyzing circulating tumor cells.

CCBIO significance
Gjertsen finds that CCBIO has been pivotal to building the projects towards the study of tumor-host interaction, exploring single cell signaling profiles in immune and tumor cells in the same sample. CCBIO has supported and built technical capacities, specifically mass cytometry for both liquid samples and tissue sections. ••

GROUP MEMBERS:

Researchers:
Gjertsen, Bjørn Tore: MD, PhD, professor, group leader
Andresen, Vibeke: MS, PhD, senior researcher
Gavasso, Sonia: MS, PhD, senior researcher
Gullaksen, Stein-Erik: MS, PhD, researcher
Hellesøy, Monica: MS, PhD, researcher
Hovland, Randi: MS, PhD, associate professor
Jebsen, Nina Louise: MD, PhD, associate professor
Omsland, Maria: MS, PhD, assistant professor, HVL
Rane, Lalit Shirish: MS, PhD, researcher
Thomsen, Liv Cecilie Vestrheim: MD, PhD, researcher

PhD candidates:
Bentsen, Pål Tore: MD
Dowling, Tara: MS
Ha, Trung Quang: MD, MS
Ktoridou-Valen, Irini: MD
Marin, Oriol Castells: MS
Motzfeldt, Inga Kristine Flaaten: MS
Rana, Neha: MS
Sefland, Øystein: MD
Sletta, Kristine: MS
Tislevoll, Benedicte Sjo: MD

Master students:
Hanif, Md Abu
Poleo, Emilia Wold
Olsen, Kristin Watnedal

Technicians:
Hoang, Tuyen Thi Van: MS, PhD, head engineer
Kopperud, Reidun: MS, PhD, senior engineer
Nguyen, Rebecca: laboratory technician

ODDBJØRN STRAUME

T3

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

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

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

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

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

Important results
1. The trial enrolled the last patient in June 2022, and further enrollment is stopped. Five regional centers included patients. After the outbreak of the COVID-19 pandemic, enrollment was significantly slowed down but was picked up again. The group is in the process of 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. Results indicate that safety and efficacy are comparable to randomized phase III trials and suggest that the use of ipilimumab can be based on current cost-benefit estimates. The group has collected tissue samples from primary tumors and pre-treatment metastatic biopsies and started to analyze the material for predictive markers.

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. The group is the first to show a correlation between strong expression of the β2-adrenergic receptor and clinical benefit from bevacizumab in melanoma. The article is currently under review.

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. The report is currently under preparation.

Future plans
In 2022, the group received grants from The Norwegian Cancer Society as well as from Helse Vest to establish infrastructure and group competence to perform state-of-the art methodologies and computational approaches to maximize the impact of biopsy samples obtained from patients participating in clinical trials and to define a new precision medicine approach to improve immunotherapy efficacy for melanoma patients. In addition, the group has started to plan new projects focusing on adaptive mutability as a universal stress response caused by cancer treatment, driving tumor cell heterogeneity and resistance.

CCBIO significance
Straume finds that CCBIO has greatly facilitated multidisciplinary collaboration across the different programs between his group and other CCBIO groups. The scientific environment provided by the center has been inspirational and has challenged group members to think "outside the box" to find new ways to identify novel targets for therapy. Also, being part of CCBIO has been beneficial when applying for grants. ••

GROUP MEMBERS:

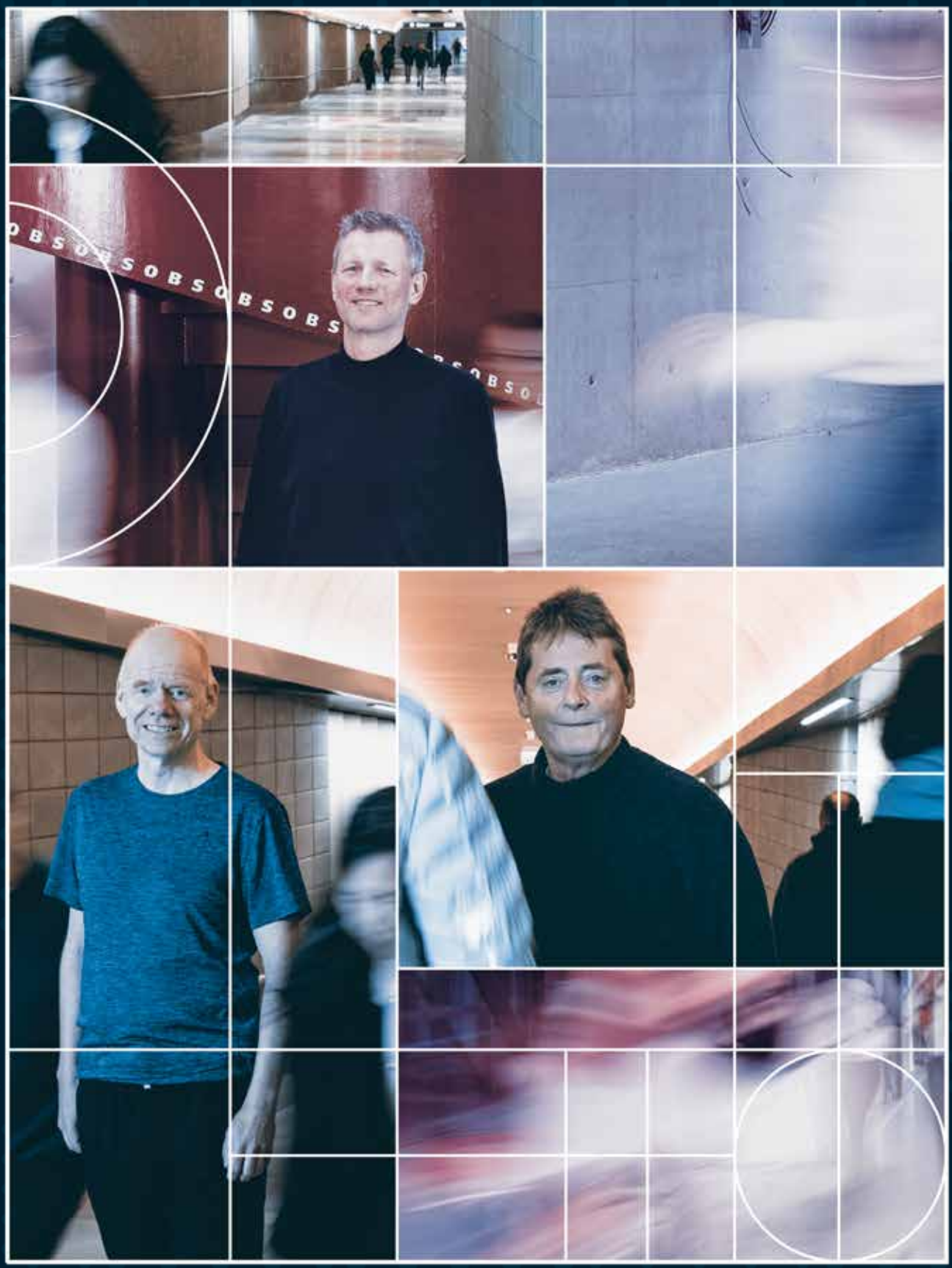
Straume, Oddbjørn: MD, PhD, professor, group leader
Dillekås, Hanna: MD, PhD, guest researcher
Kopperud, Reidun: senior engineer
Pilskog, Martin: MD, PhD, guest researcher
Schuster, Cornelia: MD, PhD, postdoc

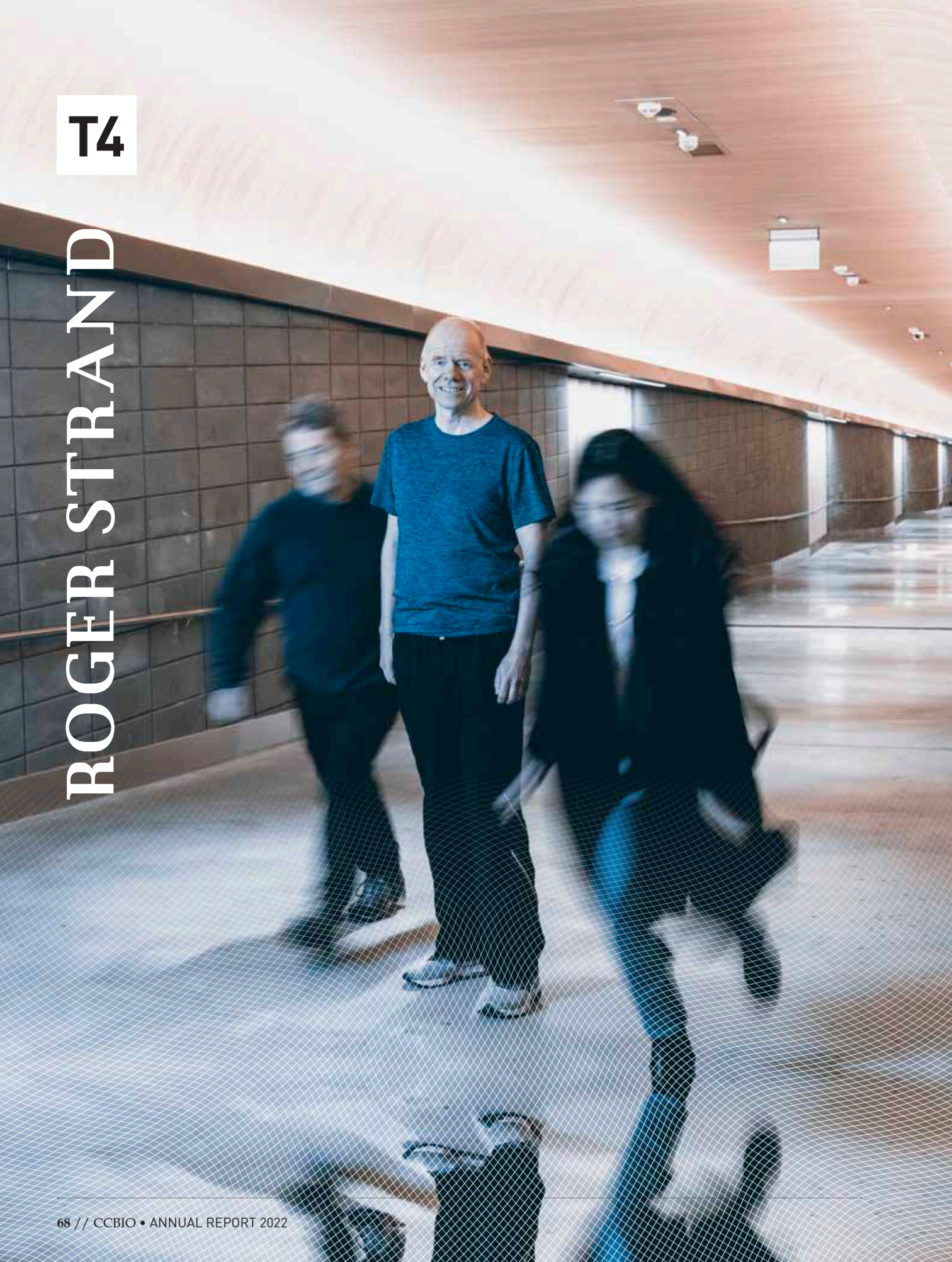
T4

TEAM 4

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 their work, and to ultimately influence the policy making and public debate 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/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).

Subprojects
CCBIO's ELSA group is a small-scale operation that can be seen as one project. They interact and are tightly linked, however, to similar RRI projects (NFR Res Publica and AFINO, and Horizon 2020 SuperMoRRI and TRANSFORM) which are also in their final phase (Res Publica and TRANSFORM being completed in 2022). 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. A particular focus in 2022 was the further development of the interdisciplinary research with Bjørge's group, and specifically Karen Gissum's PhD project that integrates dimensions from ELSA and hermeneutical health research into clinical research on ovarian cancer.

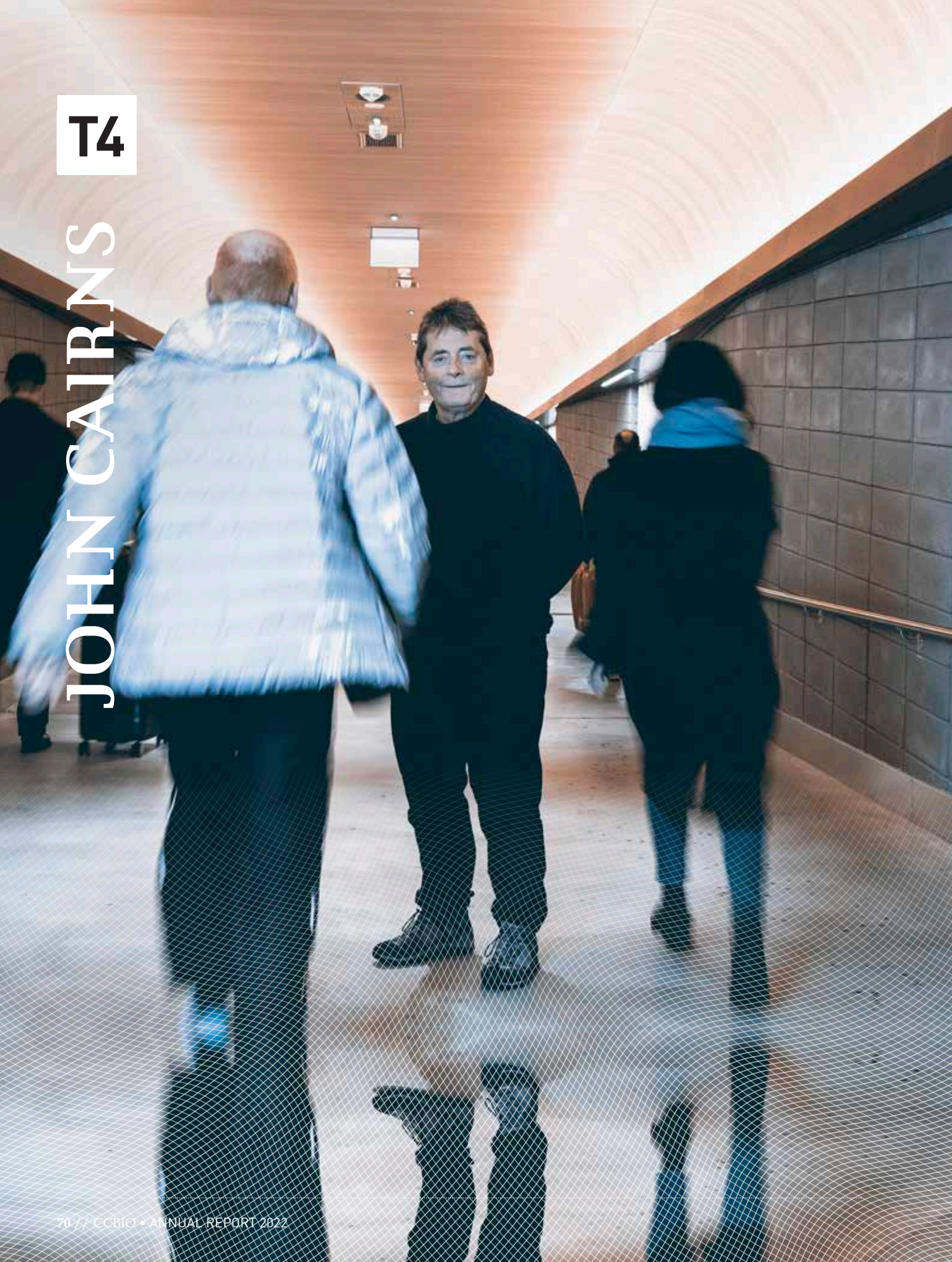
Important results
Strand's group builds insights and intellectual understanding (for peers) and ELSA/RRI awareness, within the consortium and its partners and audiences. The highlight in 2022 was the publication of an interdisciplinary research anthology "Precision Oncology and Cancer Biomarkers: Issues at Stake and Matters of Concern", edited by Anne Blanchard and Roger Strand and with 17 contributors from the CCBIO ELSA network. The key focus of the publication is the interdisciplinary analysis of the sociotechnical imaginaries of personalized and precision cancer medicine. By January 2023, the open access e-book version had registered >18k downloads.

Future plans
CCBIO is progressing through its second 5-year period. 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. 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 them 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.

CCBIO significance
ELSA research activities on cancer biomarker research and imaginaries of personalized and precision cancer medicine would not have existed without CCBIO. The center has provided both the occasion, substrate, intellectual environment and funding for this research. ••

GROUP MEMBERS:

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


T4
JOHN CAIRNS

Research focus
The Health Economics Group has 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 completed her PhD thesis entitled "Improving economic evaluation and decision-making for oncology drugs using real-world data". She built a unique database of 229 oncology appraisals undertaken by the UK-based National Institute for Health and Care Excellence (NICE) during 2011-2021, 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 thesis included papers detailing 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, and an analysis comparing the use of data in appraisals of targeted cancer therapies and non-targeted cancer therapies.

Another project has focused on the use of health economic information to inform decision making regarding the adoption of new health technologies. This included a study of how molecular targeted therapies and immune checkpoint inhibitors for the treatment of non-small cell lung cancer have been assessed.

Important results
Managed Access Agreements are being used increasingly as a means of improving access to treatments where the evidence of clinical effectiveness is too uncertain for NICE to recommend routine commissioning. The Cancer Drugs Fund (CDF) was introduced in England in 2016 to give patients access to these potentially valuable treatments. The CDF provides the drugs for several years while additional data are collected before a final review of the drug takes place. An analysis of the first twenty-four drugs to exit the CDF highlighted the important role played by longer follow-up of patients in the original clinical trials used to support the introduction of these drugs and the very limited role played by the data collected from patients receiving the drugs provided through the CDF. This is an important finding given the widespread enthusiasm for using real world data to inform drug reimbursement decisions.

Clear differences were observed between the appraisal of checkpoint inhibitors and that of molecular targeted therapies, at least in the context of non-small cell cancers. These differences derive from the more limited clinical data and the more restricted application of targeted medicines.

Future plans
Future work will involve further analysis of the rich oncology drug database, particularly focusing on the maturity of overall survival data and its impact on economic evaluation and decision making. It is planned to extend the work on molecular targeted therapies and immune checkpoint inhibitors from non-small cell lung cancer to all cancers where these treatments have been introduced. A further project will explore the economic evaluation of Antibody Drug Conjugates.

CCBIO significance
Being part of CCBIO has provided support for three PhD students to research different aspects of the economics of cancer biomarkers. Cairns finds that the partnership has also provided important repeated opportunities to discuss these economic issues with CCBIO colleagues coming from a quite different disciplinary background, and the opportunity to develop health economics teaching for non-economists. ••

GROUP MEMBERS:

Cairns, John: MA, MPhil, FRCP, professor, associate investigator, group leader
Kang, Jiyeon: PharmD, MS, PhD candidate

T4

OLE-FRITHJOF NORHEIM

Research focus
In 2022, the Bergen Centre for Ethics and Priority Setting (BCEPS+) was awarded the prestigious Centre of Excellence Status from the Norwegian Research Council. With ten-year funding, BCEPS+ aims to become a world-leading research center on ethics and priority setting.

BCEPS+ will continue to work on priority setting challenges in Norway, and the collaboration with CCBIO on cancer biomarkers, precision medicine and fair priority setting has been an important experience. In CCBIO, Norheim's group has worked on 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
Eirik Joakim Tranvåg's PhD project "Precision and Uncertainty: Cancer biomarkers and new perspectives on fairness in priority setting", with Ole Frithjof Norheim as the main supervisor, was the main subproject in Norheim's CCBIO team. Tranvåg successfully defended his thesis in September 2021. In 2022 the final article of the thesis was published (Tranvåg EJ et al., JAMA Netw Open, 2022; PMID: 35767256).

Important results
The article *Appraising Drugs Based on Cost-effectiveness and Severity of Disease in Norwegian Drug Coverage Decisions* was published in JAMA Network Open in June 2022. In the article, Tranvåg and colleagues were able to study confidential drug price information used for drug appraisals and coverage decisions in Norway. The authors demonstrated how cost-effectiveness and severity of disease are systematically implemented and used in appraisals and that the Norwegian method may be a feasible strategy to control increasing drug prices. This paper was important for Norwegian health policy discussions and received considerable media attention when published.

Future plans
The BCEPS+ Centre of Excellence will start its journey in July 2023 and expand its activities. The main aim of BCEPS+ is to develop innovative methods and a new ethical framework that can be applied at all levels to achieve fair and efficient priority setting in health.

After completing his PhD, Tranvåg now works as a senior advisor in The Norwegian Biotechnology Advisory Board, with responsibility for personalized medicine, bioethics and other relevant topics for biotechnology and ethics.

CCBIO significance
Norheim considers it to have been extremely fruitful to be part of a center where skillful and motivated researchers with different backgrounds meet and interact. Both in the ELSA group and in CCBIO in general, the sharing of experiences and knowledge has been very rewarding for the team. Also, CCBIO's faith, commitment, and willingness to invest in young researchers has been truly excellent. ••

GROUP MEMBERS:

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

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 prediction of outcome. They are currently working on a systems 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 large cohort 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 to analysis of leukemia and solid tumor data analysis where the group is now using single cell data to better dissect changes in gene expression and relations to cell types and tumor microenvironments. Jonassen contributed to a study led by the Gjertsen group showing that response to chemotherapy can be measured shortly after treatment using CYTOF, a study published in Nature Communications (early 2023).

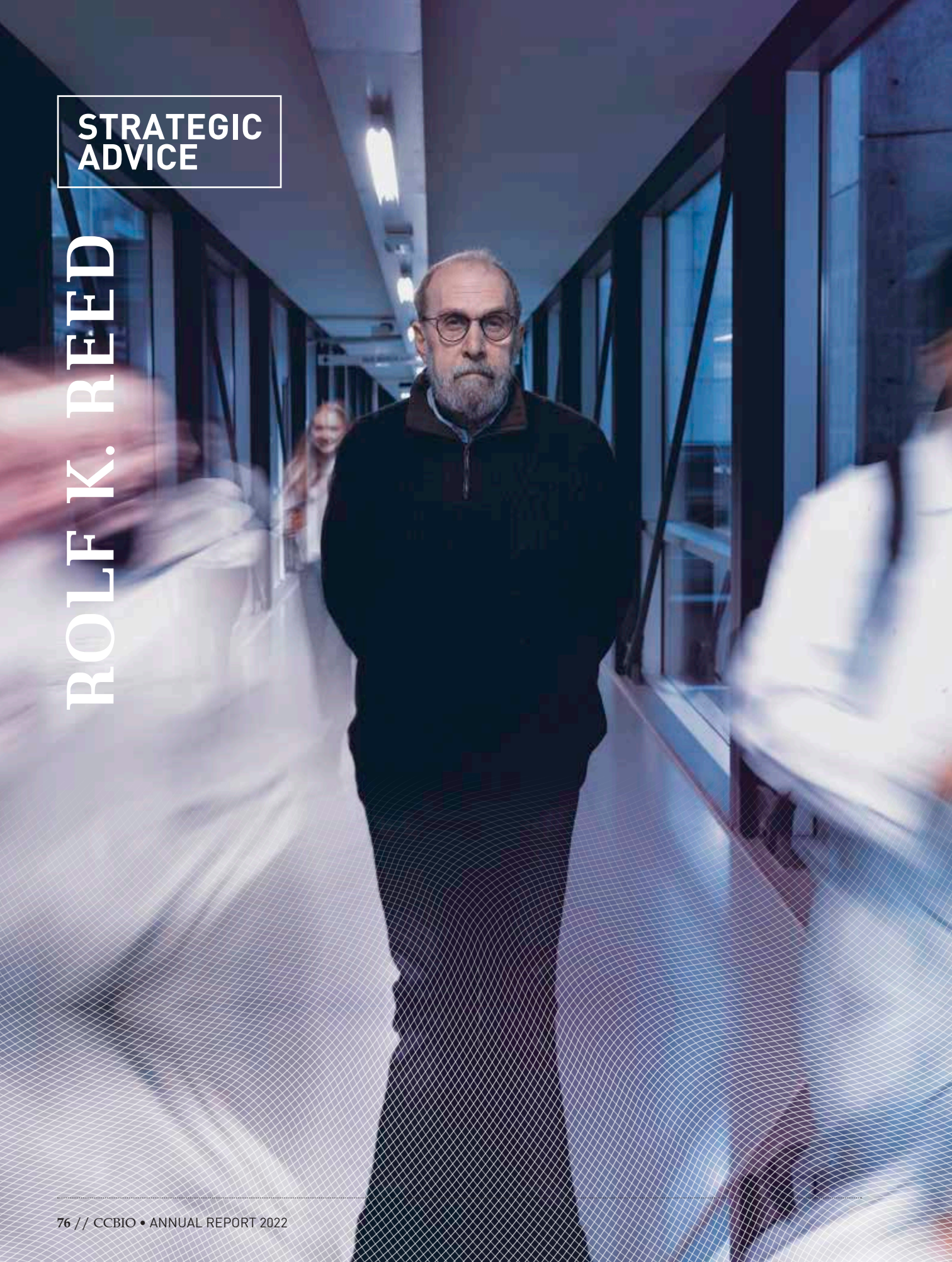
Future plans
The group will continue developing methods to utilize single-cell and high-resolution spatial data towards precision medicine. Jonassen is also increasing his engagement towards artificial intelligence and will explore ways of combining AI approaches to analyze tumor microenvironments using multi-modal information including imaging data.

CCBIO significance
For the Jonassen group, being part of CCBIO has provided opportunities to work with several cancer-oriented groups helping to guide methods development towards the real needs in cancer projects – and to engage in analysis of novel data generated in the context of CCBIO. ••

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, and he is currently affiliated to the Lorens group. Maria Tveitarås with Professor Linda Stuhr as main supervisor defended her PhD thesis in 2022 in a project investigating the role hyperbaric oxygen treatment on cancer development and metastasis in mice models of breast cancer.

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 of leadership positions and strategic committees at the University of Bergen, as well as having been dean, deputy dean and head of department for many years. Reed's long experience with committees and planning groups in research councils, international evaluation and advisory boards is brought into the longtime strategic planning in CCBIO, both for the remaining duration of the Centre as well as for the continuation when the ten-year core funding from The Research Council of Norway expires in 2023.

Among the commissions of trust held by Reed in recent years, were chair of the board at the Center for Advanced Studies at the Norwegian Academy of Science and Letters.

Research activities

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


Bruce Zetter
Carl-Henrik Heldin
Afe van der Zee

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. The CCBIO SAB convened in-person in Bergen on June 3, 2022.

In their 2022 report, the SAB stated being very much impressed with the development of CCBIO, both in terms of its high scientific production, its extensive training programs, and dissemination efforts. They consider CCBIO to have a strong leadership who has managed to bring together scientists with complementary skills to build a strong collaborative community, creating a vibrant scientific atmosphere.

The SAB was reassured by the fact that CCBIO, despite the sequela of the pandemic, has been able to retain the motivation and enthusiasm for high-level translation of findings from the lab to the clinic. CCBIO's large number of clinical trials, in particular in leukemias, gynecological cancers, prostate cancer and melanoma, speaks for this. The SAB was impressed by the work of the new junior faculty members Carina Strell and Agnete Engelsen, their work being highly collaborative and synergistic with other CCBIO members, and a significant potential for the future. Further, the inclusion of an Ethics and Economics program is a unique strength of CCBIO, e.g. influencing members of the center and others to reflect on their work in a broader context of societal impact. The ability to get easy access to high-level support in application of bioinformatics analyses remains a problem managed by the CCBIO scientists by forming research collaborations with bioinformatics environments.

Moreover, CCBIO researchers are involved in extensive training and teaching programs. CCBIO's excellent Research School for Cancer Studies has a series of important courses, the newly established course in medical innovation being an especially commendable recent addition. Educational efforts such as these represent a significant strength and provide a clear advantage to CCBIO's younger members. The CCBIO Masterclass, aimed at training promising young future group leaders, is very well received by the SAB. They believe that this is something that could potentially be expanded with benefit to junior faculty in other programs at the University of Bergen.

The SAB enthusiastically supports the continued development of these efforts and recommends that CCBIO's educational efforts be further supported by the University of Bergen as it represents a jewel in the crown of the wider university.

Through its impressive annual report, newsletters and general outreach through the media, CCBIO has made extensive efforts to reach out to both the scientific community and the general public, providing information about its findings and activities.

In brief summary, CCBIO's first 9 years have seen an excellent research environment being established and continuously developed, with a strong collaborative consortium of skilled scientists with complementary expertise and performing excellent basic, translational and clinical science; their research efforts have resulted in a large number of important publications and excellent educational and training activities.

> **"The SAB strongly recommends the University of Bergen to continue, and if possible, increase the support for this very successful Center of Excellence." ••**

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

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.*

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 2022, CCBIO's International Faculty numbered 14 affiliated investigators, and CCBIO clearly feels that this unique group has strongly supported the center's many activities and efforts.

FRÉDÉRIC AMANT

Frédéric Amant, PhD and MD, received his medical degree from the University of Leuven (KU Leuven), Belgium in 1992, completed his specialty training in obstetrics & gynecology in 1998, and his subspecialty training in gynecologic oncology in 2000. He is specialist at the UZ Leuven, Belgium and the Netherlands Cancer Institute in Amsterdam, the Netherlands.

Frédéric Amant is currently professor at the KU Leuven, Belgium and the University of Amsterdam, the Netherlands. In Leuven he heads the scientific research section of his specialty. 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. 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. He is co-PI of the CoNteSSa-NEOCON study that explores the potential to preserve fertility in young women with cervical cancer. He is PI of the EUGENIE study in endometrial cancer, that aims to link surgical stage to the molecular classification. In addition, he is PI of the VULCANize2 study, a randomized trial that investigates the value of neoadjuvant chemotherapy for locally advanced vulvar cancer. He is co-PI of the EN2 study that investigates in a randomized setting the value of chemotherapy in early-stage high risk endometrial cancer.

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 appreciates the CCBIO collaborators and the collection they have established of endometrial cancer tissue samples with deep clinical, radiologic, and molecular characterization. Together, the hope is 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. To this end, the Beroukhim lab has hosted CCBIO researchers in Boston continuously for over a year, with plans to continue hosting Bergen-based CCBIO researchers for at least another 18 months.

MARTA BERTOLASO

Marta Bertolaso is a 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, Soft Skills 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 been working on the follow-up of the MIT volume (2021) "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 2023.

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. A 2022 publication from Brekken, Lorens and colleagues demonstrated that AXL

inhibition restores sensitivity of STK11/LKB1 mutant NSCLC to immune checkpoint blockade (Li et al., Cell Rep Med; PMID: 35492873). 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 (Sui et al., Nat Comm 2022; PMID: 36575174), 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 until 2017 the founding president of the European Translational Ovarian Cancer Network (EUTROC), 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 director 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. Recognizing significant evolutionary differences between the way humans and other animals suppress cancers, the LaBarge lab invests substantially in development of primary cell culture systems that maintain more *in vivo* like transcriptomic, epigenomic, and proteomic states in epithelial and stromal cells of breast.

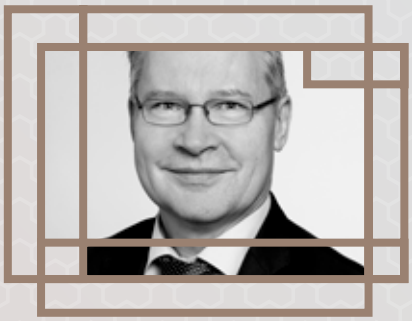
Professor LaBarge has a long-term collaboration with Professor James Lorens. Their teams have been using high-dimensional single cell CyTOF-based analyses to quantify phenotypic changes in human mammary epithelia with age. They find that the most significant changes that arise with age are in a core 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. Most recently the LaBarge and Lorens labs have focused their collaborative analyses on understanding the impacts of age-dependent changes in cytokeratin expression, and how that rewires signaling pathways, in luminal cells of cancer susceptible women. They have published additional works reporting novel methods for examining microenvironment effects at single cell resolution, and the role of Axl in mammary stem cell differentiation.

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 2022, 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 used spatial transcriptomics to identify copy number variations within prostate tissue that are conserved between histopathologically benign and cancer regions implying that some genomic events are early evolutionary traits. Biologically, Mills and collaborators continue to study the impact of glycosylation on the stability and activity of key oncogenes and tumor suppressors, reporting this year that p53 stability and function are affected. Finally, Mills and collaborators have continued a research project to applying light sheet microscopy to human tumor samples to generate 3D/high-depth imaging data on biopsy samples with the aim of enhancing 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 at Cancer Immunology Immunotherapy with colleagues from CCBIO. 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 22, 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 2022 he stepped down as Director. 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, Fellow of the American Association for the Advancement of Sciences, and member of Academia Europaea. He has published over 285 papers and edited several books/journal issues. He has an H-index of 114 and is always in the list of highest cited authors in the world.

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 and Lars A. Akslen.

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.

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.

Jean Paul Thiery is the chief scientist of Biosyngen Pte Ltd Singapore, a cell-based immunotherapy company; he is also the cofounder and chairman of Biocheetah Pte Ltd Singapore, a company focusing on the diagnostics of urological cancers. He is a scientific advisory board member of Papyrus Inc USA together with Professor James Lorens. This company is involved in elucidating the function of OPCML as a suppressor of AXL function in mesenchymal-like carcinoma.

Professor Thiery has made seminal contributions in cell adhesion, cell migration, morphogenesis, and cancer, publishing more than 510 peer-reviewed articles in different areas of the life sciences (h-index above 125). 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.

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 obtained funding from the Norwegian Cancer Society (NCS) and from Helse-Vest, for projects on identification of novel tumor stroma-derived biomarkers in breast cancer. In this area, collaborative studies with Professor Lars A. Akslen have led to patent applications and ongoing commercial development of findings. Ongoing collaborative projects exploit imaging mass cytometry for discovery of novel breast cancer niches with drug target and biomarker potential. Together with Akslen, Östman is also involved in collaborative tumor tissue profiling studies with Teijo Pellinen at the FIMM institute in Helsinki.

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, with a successful meeting held at Solstrand in November 2022.

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. ••

RESEARCH SCHOOL FOR CANCER STUDIES: COURSES AT CCBIO

The CCBIO Research School for Cancer Studies (RSCS) has a focus 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 research school 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, and the PhD candidates and postdocs get an opportunity to meet and discuss their projects across 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 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 prompted by the pandemic 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. It is our perception that open participation, also without taking ECTS, contributes towards the overall quality of our courses, benefitting CCBIO's PhD students. 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 international and national scientists from other research communities.

The RSCS now has an established collaboration with the research school at Neuro-SysMed, a center for clinical treatment research on neurological diseases. The resulting 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 2022, CCBIO held the courses that run continuously (CCBIO901 and CCBIO902), as well as CCBIO906 in February, CCBIO904 in April, CCBIO908 in May, CCBIO905 in September, and CCBIONEUR910 in November. You can read more about these activities in separate paragraphs below. For 2023, the RSCS plans to run CCBIO901 and CCBIO902 continuously as well as CCBIO907 (March), CCBIO908 (May), CCBIO903 (October and December), and CCBIONEUR911 (fall 2023). We seek to facilitate learning by the most suitable pedagogic methods, e.g., by engaging in various forms of student active/centered learning and increasing motivation by including inspirational lectures. As examples of the adapted methods, we would like to mention mixed onsite and online participation, group work solving cases and elaborating presentation (several courses) and blended learning (CCBIONEURO912) as well as integrating patient

user groups directly in the teaching (CCBIONEUR910). The most prominent examples of inspirational lectures within CCBIO RSCS are the talks by Bob Langer, the founder of Moderna, in CCBIONEUR912 and at the CCBIO Annual Symposium in 2022.

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 Blanchard and Roger Strand: "Cancer Biomarkers: Ethics, Economics and Society" (2017, Megaloceros Press), and "Precision Oncology and Cancer Biomarkers: Issues at Stake and Matters of Concern" (2022, Springer).

CCBIO903 aims to address several key questions:

- What are the promises, limitations, and consequences of the "imaginaries" 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 economic aspects.

The teaching has from the outset been highly interdisciplinary with Roger Strand from philosophy of science, Anne Blanchard from science and technology studies, John Cairns from health economics and Marta Bertolaso who co-designed new elements in 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 have been 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 was last run in the fall term of 2021, onsite participance only. The participants then 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, Anne Blanchard, Marta Bertolaso and John Cairns.

CCBIO904 – Biomarkers and Tumor Biology in Clinical Practice

CCBIO904 is a 4 ECTS course covering broad tumor biological topics that are important for understanding how cancer occurs, and the mechanisms that control tumor growth and morbidity. The course has a particular focus on biomarkers that have or may 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 approaches 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 April 20-22, 2022, as a fully digital event. 32 PhD candidates completed assignments and passed the exam. In addition, 15 were registered for non-ECTS participation for professional update only.

Oddbjørn Straume has the academic responsibility and Reidun Kopperud is the course coordinator.

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 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 covering a wide range of topics from basic techniques on nucleotides and proteins to more advanced approaches, as well as bioinformatics and biobanking. The course focuses on methods to study biomarkers in tissue samples, blood samples, circulating tumor cells and DNA, and other biological materials. Methodologies like PCR techniques, microarray, next-generation sequencing, tissue microdissection and proteomics, bioinformatics and artificial intelligence, immunohistochemistry, in situ hybridization, imaging mass cytometry, protein ligation assays, Western blot and ELISA, flow cytometry including mass cytometry, and biobanking are presented. Changes in nucleic acids and proteins in different settings are discussed, as is the clinical applications of the various methods.

The course was established in 2015 and was arranged for the 4th time September 27-29, 2022. This was the second time as a fully digital event. The course has been announced through the NorDoc network course database and is open for international participation. This year, the majority of the 83 registered students came from the universities of Bergen, Oslo and Stavanger, and several participants were from Karolinska Institute (KI) in Sweden and University of Copenhagen in Denmark, as well as participants from Italy, Pakistan, United Emirates, and Nigeria. 31 attendants claimed ECTS, the remainder attending solely for the transfer of knowledge.

A highlight of this year's course was the lecture by CCBIO international faculty Professor Klaus Pantel. He gave an inspirational talk on the promise of ctDNA and CTCs in the evaluation of cancer treatment efficacy. This lecture was opened up for a larger audience as a CCBIO Seminar, see more details in the Seminar section.

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. This work is then presented to their peers and a panel of experts. This year, the expert panel consisted of Liv Cecilie Vestrheim Thomsen, Cornelia Schüster, and Harsh Dongre, who evaluated the presentations and participated in lively discussions with the students. Based on the reflections and feedback from the students, this proved a valuable learning experience for all. The course was concluded by a three-hour multiple-choice exam.

Lars A. Akslen and Agnete Engelsen have the academic responsibility and Ingeborg Winge is the course coordinator.

CCBIO906 – Cancer Genomics

CCBIO906 is a 3 ECTS course providing a broad understanding of the main aspects of cancer genome research by next generation sequencing (NGS) technologies and associated analytical tools, and how NGS can be applied both to identify new cancer biomarkers and for diagnostics as well as treatment selection.

CCBIO906 was first held November 2017. February 23-23, 2022, the course was held for the third time, as a hybrid course with a mixture of on-site and online participants and lecturers. This did however not at all hinder active participation and interesting discussions among the 40 registered participants.

An overview of NGS methods, data sharing and data management, as well as open sources for genomic data were covered. The topics also included single cell sequencing, data analysis of whole genome data, copy number variants, RNA, and structural variants. Furthermore, as there is increasing focus on liquid biopsies in current cancer research, this topic was highly relevant for demonstrating how NGS can be implemented into the clinical work with cancer patients via clinical studies and clinical trials. The possibilities and challenges of drug repurposing and working with patients with heritable diseases and their families were also presented.

Group work is an important part of the course, and the participants did an excellent job discussing and presenting relevant topics within the field of cancer genomics, covering some of the main focus areas of the use of NGS in research settings and potential clinical applications, as well as the ethical aspects of applying new findings clinically. The participants also had the opportunity to pose questions prior to the course, and most questions were debated during the course. To pass the course and earn credits, the candidate must be present at least 90% of the course, participate actively in the group work, and pass an online exam.

In 2022, Liv Cecilie Vestrheim Thomsen and Erling Høivik were academically responsible, and Rebecca Nguyen was 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-II project "Bergen-Harvard Cancer Studies phase 2: Continued Partnership for Responsible Education, Research and Innovation Excellence." 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.

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.

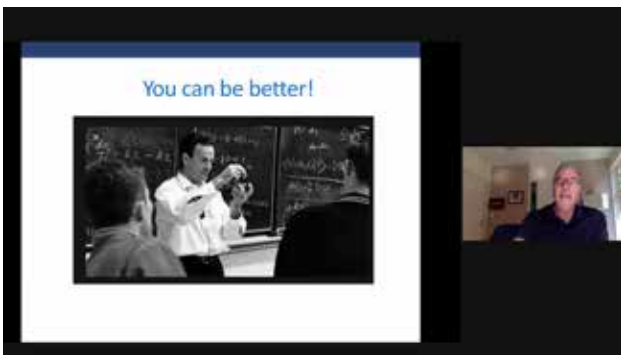
- The skills to formulate hypotheses to plan and conduct studies on cancer-related vascular biology, consider utility and limitations in use of cancer related biomarkers and be able to communicate relevant literature and methods concerning cancer related vascular biology, with critical reflection.

- 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.

Topics range from discovery to clinical application, lymph-angiogenesis and vascular biology in noncancerous 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. During each course the Harvard faculty also introduces a set of essential soft skills to the participants. In 2020 these were "Crafting a presentation", "Fundamentals of Peer Review" and "Crafting a presentation". The 2023 course will focus on "Pitch preparing", "Proposal writing" and "Mentorship".

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 arranged for the first time in 2018. Elisabeth Wik and Lars A. Akslen held the academic responsibility, with facilitation on the US side by Michael S. Rogers from the Vascular Biology Program (VBP). The last course was held September 21, October 2 and October 9, 2020, this time 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. VBP faculty contributing with lectures in 2020 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.



The course will next time be organized March 20-31, 2023, with international faculty Bruce R. Zetter, Michael S. Rogers, Randy S. Watnick, Diane R. Bielenberg, Ed Smith, and Dipak Panigrahy, in addition to CCBIO's local experts Oddbjørn Straume and Carina Strell. Agnete Engelsen and Lars A. Akslen will have the academic responsibility, with Heidrun Vethe as course coordinator.

CCBIO908 – Scientific Writing and Communication Seminar
CCBIO908 is a 2 ECTS 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. The lecturers draw from their vast experience both as writers of scientific texts and reviewers of publications. Lecturers are 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 contributes 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.

CCBIO908 was first run in December 2017 and from 2019 onwards it has been an annual event due to its popularity. It was run digitally in the pandemic and in a hybrid format in 2022. Registration was split between students wanting ECTS, and attendees participating for professional update only. Of the161 participants, 118 came from CCBIO and other programs and research groups at UiB and from other

institutions in Norway, 21 from various institutions in Denmark plus some from other Nordic countries, and the rest from institutions in Europe, Asia, Africa and the USA. 116 participated for ECTS (master students and PhD students), and 45 for non-ECTS (researchers, postdocs, and engineers).

Elisabeth Wik was academically responsible with Vandana Ardawatia and Harsh Dongre as coordinators. The next course will be in May 2023.

CCBIONEUR910 – Patient and Public Involvement in Medical and Health Research

CCBIONEUR910 is a 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 clinical 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 by educating both researchers and users in a colloquial setting.

The course was first run in 2021, and again November 30 - December 2, 2022. It encompasses a broad spectrum of national and international lectures from researcher and user organizations, the Norwegian Research Council, 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.

A panel debate including Nikolai Raabye Haugen, Gunnhild Berglen, Caroline Engen, Nina Grytten Torkildsen and Kristin Tuven discussing different perspectives on ethical challenges and practical implementation of patient and public involvement, was engaging to the audience.

Group sessions included both pre-arranged case discussions as well as each research school participant 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. Eitri Medical Incubator was a great venue for the group sessions and the final day with lectures and panel debate.

Of the 59 participants, 29 were user participants from a wide variety of user organizations. Among the 30 researcher participants, around two thirds were PhD candidates, and the rest were researchers and 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 Rasmus Humlevik (CCBIO) are the course coordinators.

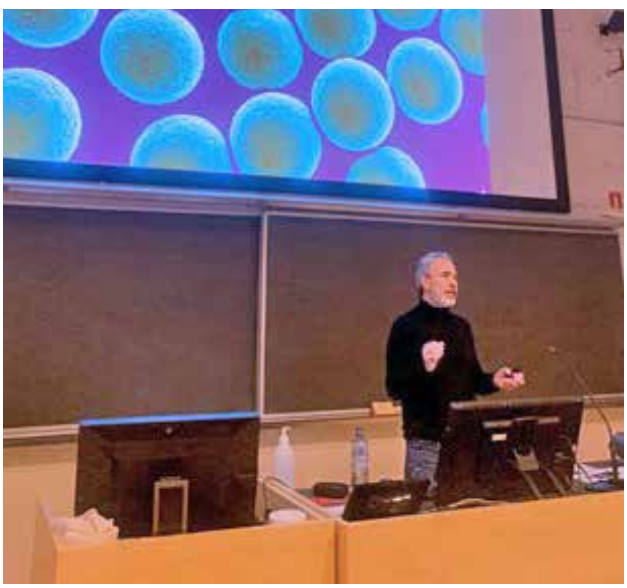
CCBIONEUR911 – Clinical Trials in Cancer Research
CCBIONEUR911 is a new 2 ECTS course on clinical trials. The course is based on a course qualifying for a Good Clinical Practice (GCP) certificate held in 2019, at that time organized by Line Bjørge and Hani Gabra. It has since been expanded as a collaborative effort with Neuro-SysMed, held 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 interventions. 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 most recent 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. The next course is planned for the fall of 2023.



CCBIONEUR912 – Health Innovation Course
CCBIONEUR912 is the first PhD course at the UiB with a focus on health innovation and was arranged for the first time in 2021. This course provides an invaluable opportunity, especially for early career medical researchers, to gain insights on how to bring research to society and offer perspectives on alternative entrepreneurial career paths. The overall aim of this course is to encourage and enable PhD students and young researchers to identify and evaluate their own research projects' innovation potential. The course consists of two modules over a total of 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 provides inspiring lectures by people who have walked this path before them, and thus various routes to exploitation of research-driven innovations. 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 into what it takes to make a successful company like Kinn Therapeutics in addition to running a research lab, and Karl Henning Kalland presented his research and the exciting work of the company he founded, Alden Cancer Therapy II.

An absolute highlight was the inspirational keynote lecture by Professor Robert Langer, researcher and co-founder of the biotech-company Moderna, with a talk on his successful career path. He encouraged the participants to look for good role models, endure criticism and think big. 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. 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 encouraged 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.

The course was last run November 8-9 and December 2-3, 2021, with onsite participation by 18 participants. The participants were a good blend of researchers from different backgrounds, such as natural scientists and medical doctors, consultants in oncology and students from the faculty's Medical Student Research Program.

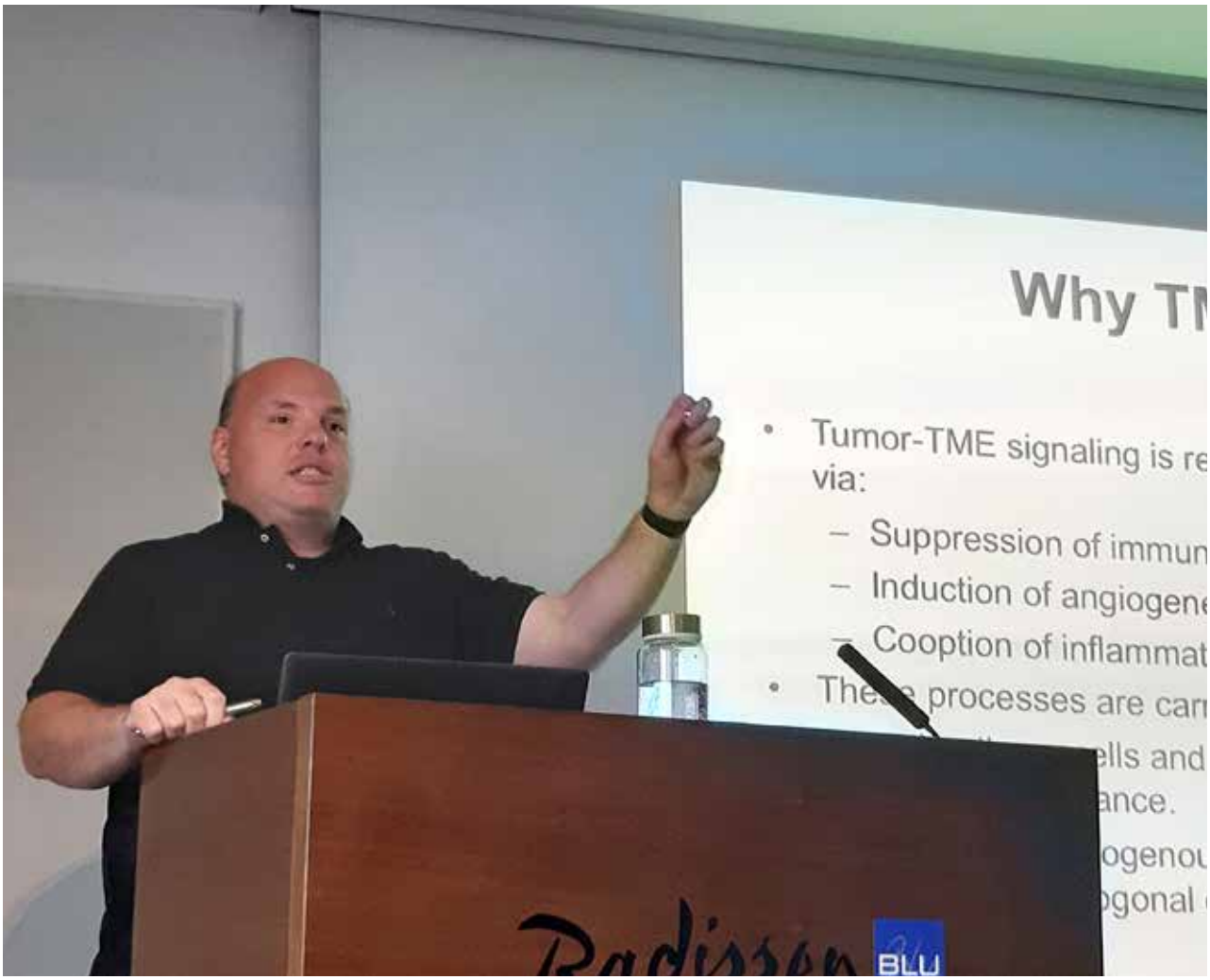
Agnete Engelsen (CCBIO) and Magnus Alvestad (Neuro-SysMed) had the academic responsibility for CCBIONEUR912 in 2021/22, and Ning Lu (CCBIO) and Hilde Norborg (Neuro-SysMed) were the course coordinators.

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 and 2019, three PhD students visited each year the labs of Randy Watnick, Marsha A. Moses, Diane Bielenberg, and Michael Rogers. The students were warmly welcomed by the PIs and other colleagues at the host labs and learned a range of different lab techniques and improved their presentation skills and critical paper reading.

Due to the pandemic, the program was on hold throughout 2020-2022, but will from 2023 again be up and running – three CCBIO students leaving for a 12 weeks' visit in January. 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 Boston visits. Networking with students and faculty at the VBP is rewarding for the students, and of great value for their research careers.

International Collaboration and Further Development of Courses
As part of its strategic emphasis on internationalization, CCBIO 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 aggregate, 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 Research Council of Norway (RCN) and the Directorate for Higher Education and Skills (HK-dir), called International Partnerships for Excellent Education and Research (INTPART), has been running since 2017. The basis for the project was a reinforcement of existing collaborations between CCBIO and Boston Children's Hospital and Harvard Medical School, and Harvard Kennedy School. The INTPART activities are used to foster stronger integration between excellent teaching and research environments in collaboration with international partners. In addition to including master level students into CCBIO RSCS courses, CCBIO has established the new INTPART courses CCBIO907 Cancer-Related Vascular Biology, CCBIO908 Scientific Writing & Communication, CCBIONEUR912 Health Innovation, the workshop on design principles with EMBO, the Boston Lab Visit Program, the CCBIO – VBP Research Meeting at Iceland, 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. In 2020, CCBIO's application for renewed funding of its INTPART project received excellent reviews and a further three years of funding. The aim for this INTPART phase 2 project is to continue, consolidate, and further expand on the activities successfully established during the first INTPART project.

Lars A. Akslen and Marsha A. Moses (Director, VBP) are the INTPART project leaders, Elisabeth Wik has in 2017-2022 been the main coordinator in Bergen and Randy Watnick the coordinator in Boston. From the fall of 2022, Agnete Engelsen is the main coordinator in Bergen, with Michael Rogers and Randy Watnick as coordinators at VBP. For CCBIO907 and the CCBIO-VBP Research Meeting at Iceland in 2019, Michael Rogers is the VBP coordinator.

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. ••


FLUIDIGM

CCBIO
RESEARCH SCHOOL
FOR CANCER STUDIES

JUNIOR SCIENTIST SYMPOSIUM

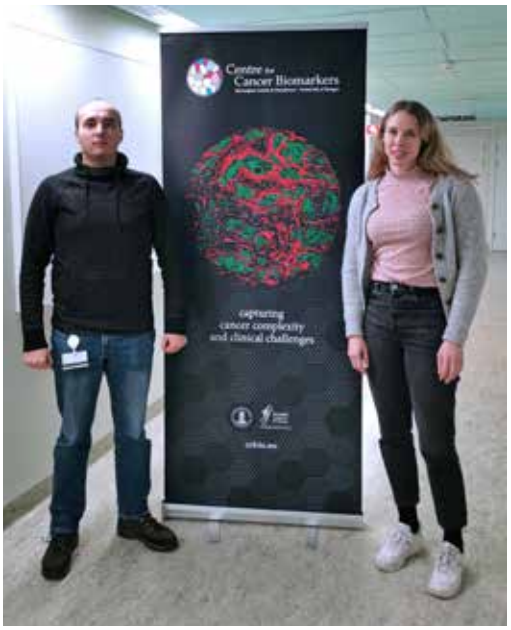
The **CCBIO Junior Scientist Symposium (JUSS)** takes place four times a year and is part of the CCBIO Research School as the course CCBIO901. Junior scientists are invited to present their research in an academic environment, thus providing the opportunity for feedback across disciplines. Notably, the symposium acts as a training arena for younger colleagues to organize the meetings and chair the sessions. 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, young researchers 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 of their daily work. CCBIO901 provides 3 ECTS for students who are required to give one oral presentation based on their own work, to actively participate in at least four symposia, and to write four reports summarizing four different presentations.

After two years with COVID-19 restrictions allowing digital meetings only, the organizers were happy to finally return to in-person attendance from 2022. The two meetings in the spring term were held as hybrid events. From the fall of 2022 and onwards, we returned to the in-person format, thereby better enabling fruitful discussions and informal interaction and networking which are important parts of the JUSS concept.

Each JUSS included presentations from students, PhD candidates and postdoctoral fellows or other researchers at an early career stage. In addition, the symposia featured keynote presentations from experienced researchers. The first keynote speaker in 2022 was Professor Klaus Pantel, a pioneer in the field of circulating tumor cells and molecules. He presented an exciting story about how liquid biopsy has moved from discovery to clinical implementation. The next keynote was held by researcher Henriette Christie Ertsås, focusing on the hot topic of predatory journals entitled: "Of course, you would never publish in a predatory journal... or would you?". In October, one of the JUSS organizers Vladan Milosevic gave a lecture about the power of mass cytometry, providing a basic introduction to CCBIO's Hyperion Imaging System and the opportunities it offers for unraveling the complexity of the tumor microenvironment in cancer research. Finally, Camilla Krakstad gave an inspirational talk on early career planning and international mobility.

In spring 2022, the Junior Scientist Symposia were organized and chaired by Cornelia Schuster, Maria Lotsberg and Hanna Dillekås. From August 2022, Vladan Milosevic and Mari Kyllesø Halle were phased in as organizers. ••


Centre for
Cancer Biomarkers
capturing
cancer complexity
and clinical challenges


FORSKNING
TIL FOLKET

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
March 10, 2022

Hybrid event: Auditorium 4, BBB, and in Zoom.

Symposium chairs:
Maria Lie Lotsberg and Hanna Dillekås.

09:00-09:15	Introduction
09:15-10:00	Keynote lecture by Professor Klaus Pantel: "Liquid Biopsy: From Discovery to Clinical Implementation"
10:00-10:30	**Coffee**
10:30-10:55	Christina Engebrethsen: "Personalized treatment for HR+/ HER2- locally advanced breast cancer"
10:55-11:20	Sturla Grøndal: "Studying cell population dynamics in kidney fibrosis with mass cytometry"
11:20-12:00	**Lunch**
12:00-12:25	Sina Takle: "Pipeline for spatial analysis of the tumor microenvironment"
12:25-12:50	Maria Omsland: "Investigation of a Nilotinib resistant CML cell line"
12:50-13:00	Concluding remarks

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
May 12, 2022

Hybrid event: Auditorium Glasblokkene, and in Zoom.

Symposium chairs:
Maria Lie Lotsberg and Hanna Dillekås.

09:00-09:15	Introduction
09:15-10:00	Keynote lecture by Henriette Christie Ertsås: "Of course, you would never publish in a predatory journal... or would you?"
10:00-10:35	**Coffee**
10:35-11:00	Amalie Fagerli Tegnander: "Low Anterior gradient 2 (AGR2) relates to aggressive tumor features in breast cancer"
11:00-11:45	**Lunch**
11:45-12:10	Maria Kathrine Tveitarås: "Suppression of breast cancer metastasis by targeting tumor hypoxia?"
12:10-12:35	Lena Hansen: "Fantastic antibodies and where to find them"
12:35-12:45	Concluding remarks

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
October 6, 2022

B301, Sentralblokka, Haukeland University Hospital

Symposium chairs:
Mari Kyllesø Halle, Cornelia Schuster and Vladan Milosevic

09:00-09:15	Introduction
09:15-10:00	Keynote lecture by Vladan Milosevic: "Multiplex profiling of the tumor microenvironment in breast cancer – Unlocking the power of mass cytometry"
10:00-10:20	**Coffee**
10:20-10:45	Harsh Dongre: "Tumor-fibroblast interactions in squamous cell carcinomas"
10:45-11:10	Tara Dowling: "Mimicking clonal architecture in Acute Myeloid Leukemia (AML)"
11:10-12:00	**Lunch**
12:00-12:25	Margunn Bye Tøsdal: "Graviclot; Changes in coagulation activation in pregnancy and the puerperium in women with mild risk factors for venous thromboembolism"
12:25-12:50	Christiane Helgestad Gjerde: "Establishment of peritoneal dECM scaffolds for culture of ovarian cancer organoids"
12:50-13:00	Concluding remarks

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM
December 8, 2022

B302, Sentralblokka, Haukeland University Hospital

Symposium chairs:
Mari Kyllesø Halle and Vladan Milosevic

09:00-09:15	Introduction
09:15-10:00	Keynote lecture by Camilla Krakstad:"Added value of international mobility?"
10:00-10:20	**Coffee**
10:20-10:45	Irini Ktoridou-Valen: "Actinomycin D treatment in patients with NPM1- mutated acute myeloid leukemia (AML) and other myeloid malignancies in Impress Norway"
10:45-11:10	Rasmus Humlevik: "Breast cancer of the young points to age-related phenotypes"
11:10-12:00	**Lunch**
12:00-12:25	Ege Solel: "Impact of cell death on glioblastoma, its tumor microenvironment and immune response"
12:25-12:50	Elaheh Javadi Arjmand: "Emotional eating and changes in dietary patterns linked to psychological distress and worries"
12:50-13:00:	Concluding remarks

CCBIO
RESEARCH SCHOOL
FOR CANCER STUDIES

CCBIO MASTERCLASS PROGRAM

The CCBIO Masterclass training program aims to ready up-and-coming post-PhD researchers for a successful transition from being part of a research group, to establishing their independent research profiles, funding portfolios and finally – their own research groups. Each Masterclass class consists of 8-10 researchers who receive individual mentoring as well as a total of 7 plenary workshops over one academic year.

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. The plenary workshops 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 group leader
- Establishing research collaborations and networks
- Science communication

Throughout the workshops, the candidates receive targeted input from CCBIO's PIs, network, and administration, as well as from staff of the Medical Faculty, The University of Bergen'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 was in 2022 coordinated by CCBIO's Research Advisor Yamila Torres Cleuren and Director Lars A. Akslen.

In March 2022, the first group of 8 candidates had their last ordinary session, focused on science communication. Communications Advisor Marion Solheim, a former NRK journalist, and Lars A. Akslen held a workshop on how to interact successfully with the mass media from the journalist and the scientist's perspective. Åshild Nylund from the University of Bergen's Communications Division provided useful advice on how scientists can promote themselves online, and Caroline Armitage from the University Library focused on profiles, publishing statistics and monitoring outreach. The final two-day workshop at Solstrand took place in late April and focused on summarizing the experiences and hammer out concrete career plans for each candidate. Each candidate presented their career plans for review and discussion by the CCBIO PIs and management, as well as their peers, before enjoying an inspirational talk by Professor Kenneth Hugdahl, UiB. The second day was dedicated to coaching on what it takes to get tenure tracked, and a thorough plenary discussion taking its point of departure in an anonymized feedback survey. The feedback was mostly positive, and also very constructive and useful for the further development of the Masterclass program. Following the end of the first batch of CCBIO's Masterclass in 2021, the candidates were granted 50 000 NOK each to spend on career building activities of their choice. They also opted to build on their experiences and tightly knit network by meeting regularly for deliberations and mutual support.

Based on the experiences gained, this year, the second CCBIO Masterclass group was launched in September 2022 by a session held by Yamila T. Cleuren, presenting the Masterclass concept and introducing the 10 new candidates to each other, presenting themselves and their future ambitions, as well as providing an overview of expectations at each career stage, drafting CVs and the benefits of mentoring.

In October, the candidates' attention was focused on how to establish and run a research group. In addition to the introduction by Cleuren, Lars A. Akslen and Daniela Costea coached on how to form the right team and find the right team members, and the tasks of a group leader, respectively.

Based on the experiences from the first Masterclass group, the session on grant applications and opportunities was this time held later, in November, rather than at the beginning. As well as Cleuren, a research advisor focused on grants sharing her accumulated experience in grant writing, the Masterclass alumni Harsh Dongre and Heidrun Vethe shared their own experiences. More specifically, this very important session covered topics like: Identifying relevant opportunities, main funding agencies, the individual parts of an application, collaborators and partners, grant writing logistics and focus on cutting-edge research and innovation.

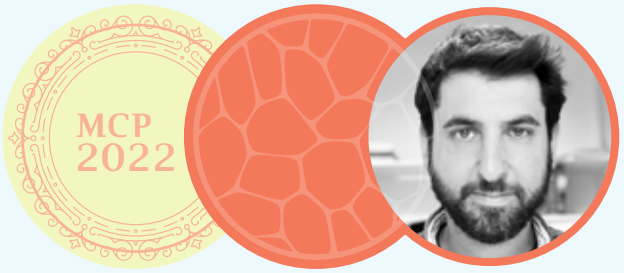
The December session focused in detail on how to conceptualize a research project. Professor Charalampos (Haris) Tzoulis from Neuro-SysMed and CCBIO's Line Bjørge held an interactive workshop focused on the process from idea to execution and the translation from basic research to clinical studies including trials.

The CCBIO Masterclass Program has received positive feedback from the participants, their mentors and CCBIO's research groups as well as the CCBIO SAB. In the evaluation of the first Masterclass, the participants stated that it would be worthwhile for universities to have similar coaching arrangements tailored for each career stage, from the early PhD-level and onwards. Small, close-knit groups, by their very nature, also forward the establishment of lasting relations and new scientific collaborations. Both mentors and mentees benefit greatly from interacting in defined roles across groups and levels of seniority, and several have continued their meetings after the expiry of the first Masterclass period.

The current Masterclass group will continue until the expiry of CCBIO's CoE period in mid-2023, continuously benefitting 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. CCBIO hopes to be able to continue to jump-start early-stage researchers in this way, making a lasting impact on individual careers and research groups alike. This is however subject to CCBIO's funding situation during its continuation phase. ••

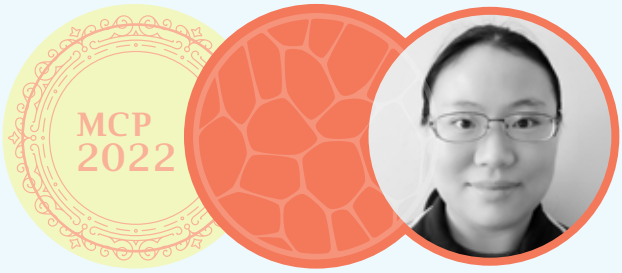
The 2022 Masterclass candidates

HEGE FREDRIKSEN BERG holds a PhD from the University of Bergen focused on organoid models and novel biomarkers for endometrial cancer. She is currently a postdoctoral fellow in the Krakstad group where she is working on preclinical modeling and drug resistance. Currently, Berg is studying chemo-resistance in endometrial cancer. The project combines patient data and functional genomic screening of organoid models to identify the molecular drivers of resistance to carboplatin. As part of this project, Berg recently completed the first part of a research stay at Dana-Farber Cancer Institute and Broad Institute of MIT and Harvard. She hopes to identify targetable alterations that can improve the efficacy of platinum-based drugs and ultimately improve outcomes for advanced and metastatic cancer. After her postdoc, she aims to secure funding for her research to establish independency with the long-term goal of leading her own research team.

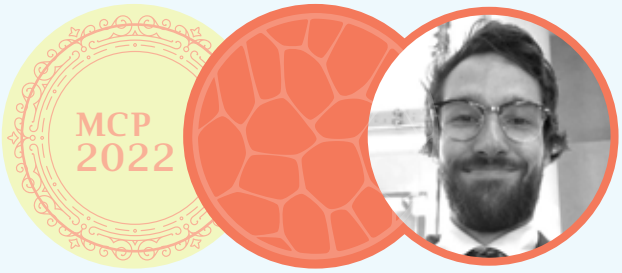


MANUEL CARRASCO holds a PhD in developmental biology from the Andalusian Molecular Biology and Regenerative Medicine Centre (CABIMER) in Spain. Thereafter he did a postdoctoral training with Helge Ræder at the University of Bergen on stem cells and diabetes. Carrasco is currently a researcher in the Akslen lab, where he focuses on the nerve involvement in breast cancer progression. He uses organoids as a model system to study the interactions of breast cancer with components of the tumor microenvironment, including nerves and autonomic signaling. He aspires to understand the interplay between tumor cells and nerves in breast cancer from multiple perspectives, leveraging his background as both a pharmacist and developmental biologist. His long-term aim is to secure funding to create a research group and establish collaborations with other research groups that provide complementary points of view on this topic.

CHRISTIANE GJERDE has an MD from the University of Bergen, where she also completed the Medical Student Research Program. She is currently a late-stage PhD student in the McCormack and Bjørge groups. The focus of her research is development of *in vitro* 3D models for ovarian cancer. The goal is to establish patient-derived organoids on decellularized peritoneal scaffolds to create a model that better represents the tumor microenvironment of ovarian carcinoma, with the hope that the model can be used to study tumor biology and evaluate new therapies. Gjerde was recently awarded NOK 200 000 from the Kolbjørn Brambani Cancer Research Fund to support her PhD project. Her long-term professional goal is to establish her own group with focus on translational cancer research.

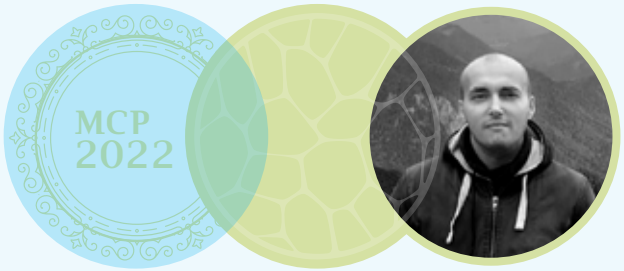


YAPING HUA received her PhD at the University of Bergen in 2020. Currently, she is a postdoc in Karl-Henning Kalland's group and will later conduct a research stay at Harvard Medical School. The theme of her project is the discovery of novel potential anti-cancer compounds and the identification of corresponding molecular targets in human prostate cancer cells. This innovative project strategy combines cancer cell cryoimmunotherapy with exclusively available panels of biologically active compounds that are isolated from medicinal herbs and plants (phytochemicals). Yaping Hua will continue the collaboration with the Harvard/Shanghai/Bergen groups to develop novel small molecular compounds and identify effects on signal transduction pathways as well as target and mechanism validation in immune cells and cancer cells. This collaborative project will benefit her as an independent group leader in the future.

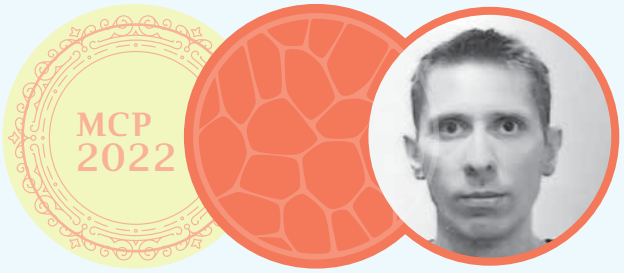


STEIN-ERIK GULLAKSEN has a master in nanotechnology and microfluidics, followed by a PhD from the University of Bergen on high dimensional single cell analysis of blood samples using mass cytometry. This work is continued in his current position as a researcher where he is analyzing samples from patients with leukemia enrolled in international clinical trials. His aim is to generate profiles of the therapy-induced changes in both leukemic and host immune cells after only hours and days since starting therapy. The goal is then to leverage these changes against clinical data to identify biomarkers that identify poor responders and possibly predict side effects. The focus is on early time points after starting therapy: hours to days after start of therapy. Gullaksen aims to achieve scientific independence as a young investigator by combining multidisciplinary skill sets with a focus on a growing repertoire of cutting-edge single cell technologies in the field of hemato-oncology.

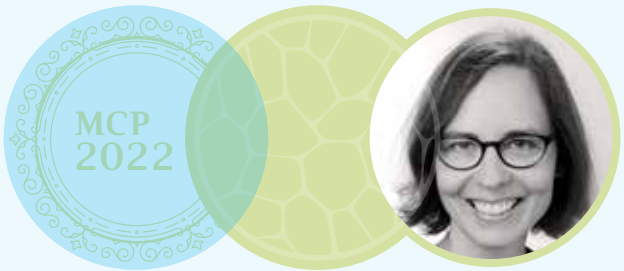
ERLING A. HØIVIK has a PhD in molecular biology from the University of Bergen at the Department of Biomedicine. He has an extensive background as a researcher within female cancers under the CCBIO umbrella. First, through previous work in the Bergen Gynecological Cancer Research Group, and now in his current position in the Breast Cancer Research Group of Elisabeth Wik. His research interest is particularly centered around younger breast cancer patients, where he uses multiangled "omics"-approaches, including epigenetics, genomics and transcriptomics characterizations. By these explorative approaches, he aims to identify and characterize new biomarkers to improve cancer treatment for this patient group and make an impact in the research field.



VLADAN MILOSEVIC holds a 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 phenotypes of these aggressive tumors. 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-multiplexed profiling of the tumor microenvironment using the Hyperion imaging mass cytometry platform. His long-term goals are to establish his own research group in the field of molecular medicine and cancer research and to pursue a clinical career in pathology.



CÉDRIC ZELTZ has a PhD in molecular and cellular biology from the University of Reims Champagne-Ardenne, France, focusing on melanoma inhibition. He is currently a researcher in the Gullberg group. For over a decade, his research was essentially based on the interactions between cells and the extracellular matrix, and on the determination of biomarkers and potential therapeutic targets in tissue and tumor fibrosis. During his postdoc in the Princess Margaret Cancer Centre in Toronto, Cédric investigated the heterogeneity of cancer-associated fibroblasts in non-small cell lung carcinoma, and he established 3D co-culture models of tumor and stromal cells. His current project focuses on new integrin alpha11 mouse models for stroma targeting. His long-term professional goal is to establish his own research group in the field of tissue and tumor fibrosis. ••



CORNELIA SCHUSTER has a PhD from the University of Bergen on predictive markers in melanoma treatment. She is currently a postdoc in the Straume and Akslen groups and focuses on identifying predictive markers for response to immunotherapy in melanoma. Her work includes both retrospective series and a prospective clinical trial led by Professor Straume at Haukeland University Hospital. Her special interest is on the impact of adrenergic signaling in cancer progression and resistance to therapy. As a medical oncologist, she has broad experience in treating melanoma patients and clearly sees the urgent need of validated predictive markers for response and the risk of developing severe side-effects in the era of immune checkpoint blockade. Her aim is to combine clinical work and translational research to contribute to optimized personalized medicine.

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 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 contacts and 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.

During the pandemic, CCBIO seminars were held digitally since gathering CCBIO would mean mustering staff from a wide array of hospital departments. In retrospect, this rather conservative approach turned out to be well founded also during the periods with a low degree of contagion. Following the re-opening in Norway in February, we carried out a gradual transition to in-person events as international travel was still curtailed or cumbersome. From the spring of 2022, we were delighted to be back in normal operation with each seminar being 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. The increased level of digitalization attained during the pandemic enabled us to run selected events as hybrids with a flexible combination of online and on-site speakers and attendants.

The seminar series forms part of the PhD-level course CCBIO902 with Donald Gullberg, James Lorens and Lars A. Akslen as academically responsible. Until 2022, the seminars were coordinated by Eli Synnøve Vidhammer, our web and newsletter editor, before leaving the helm to PhD Candidate Camilla Tvedt Ekanger for the years to come. The CCBIO seminars are also a part of the master-level course BMED380. 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 2022

Following the re-opening of Norway in early 2022, all but one CCBIO seminar were held in-person with an informal pizza get-together following the seminars. CCBIO faculty and other invited international speakers provided interesting and wide-spanning topics throughout the year. The welcoming seminar for Carina Strell provided an extended focus on breast cancer, celebrating the TMS Starting Grant enabling her to establish a research group at CCBIO.

FEBRYARY 17, 2022

Kaisa Lehti, Department of Biomedical Laboratory Science, Norwegian University of Science and Technology (NTNU), Trondheim, Norway: Crosstalk of desmoplastic tumor microenvironment and ovarian cancer in metastasis and therapy resistance. Chair: Line Bjørge.

MARCH 31, 2022

Shin Kaneko, Department of Cell Growth and Differentiation, Center for iPS Cell Research and Application (CiRA), Kyoto University, Kyoto City, Japan: iPSC-based killer cell regeneration for cancer immunotherapy. Chair: Jim Lorens.

APRIL 28, 2022

Therese Sørlie, CCBIO International Faculty, Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital, and Institute of Clinical Medicine, University of Oslo: FGFR1 as a biomarker and target for therapy in hormone receptor positive breast cancer. Chair: Lars A. Akslen.

JUNE 13, 2022

Torsten O. Nielsen, Professor of Pathology & Laboratory Medicine, MD/PhD Program Director, Faculty of Medicine, University of British Columbia, Canada: Breast cancer biomarker development: intrinsic subtypes, Ki67 and proteomics. Chair: Lars A. Akslen.

AUGUST 25, 2022

Carina Strell, Department of Clinical Medicine and CCBIO, University of Bergen. Welcoming seminar for Carina Strell on the topic Perspectives on early breast cancer – molecular biology and epidemiology. Presentations by **Carina Strell**, **Therese Sørlie and Solveig Hofvind.** Chair: Lars A. Akslen. See details in the section Special Seminars and Meetings.

SEPTEMBER 29, 2022

Klaus Pantel, CCBIO International Faculty, Director of the Institute of Tumor Biology, Center for Experimental Medicine, UKE Hamburg, Germany: The promise of ctDNA and CTCs in the evaluation of cancer treatment efficacy. Chair: Agnete Engelsen.

OCTOBER 27, 2022

Ingeborg Tinhofer-Keilholz, Department of Radiooncology and Radiotherapy, Charité-Universitätsmedizin Berlin, Germany: Advanced animal-free preclinical models for head and neck cancer. Chair: Daniela E. Costea.

NOVEMBER 24, 2022

Donald Gullberg, CCBIO PI and Professor at the Department of Biomedicine, University of Bergen, Norway: Advances in fibroblast biology. Chair: Donald Gullberg.

DECEMBER 15, 2022

Tim Coorens, Broad Institute of MIT and Harvard, USA: Using somatic mutations to reconstruct the life histories of normal and cancer cells. Chair: Camilla Krakstad.

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 2022 was still strongly influenced by the pandemic restrictions still partly in place internationally, whereas the activity picked up gradually throughout the autumn of 2022.

CCBIO Special Seminar "Can science make sense of life?" June 10, 2022, CCBIO and the Holberg Prize hosted a Special Seminar with the 2022 Holberg Laureate, **Sheila Jasanoff** (Harvard University) in conversation with **Stephen Hilgartner** (Cornell University). The seminar was chaired by CCBIO PI **Roger Strand**. The Holberg Prize is a highly prestigious prize awarded annually to scholars who have made outstanding contributions to research in the humanities, social sciences, law or theology, and the objective of the prize is to increase awareness of the value of academic scholarship from these fields. Science and Technology Studies (STS) pioneer Sheila Jasanoff received the prize for her groundbreaking research in the field. CCBIO's ELSA group has been fortunate to enjoy Professor Jasanoff's continued support, intellectually as well as institutionally, for many years.

The seminar was called "*Can science make sense of life*?", referring to Jasanoff's recent and eponymous book. This was the first time the Faculty of Medicine had the opportunity to welcome a Holberg prize winner. More than 110 people from the medical research community and several other fields at the University of Bergen embraced this occasion to gain new insights on their research.

The event focused on the social dimensions and politics of biomedicine and biotechnology, with the arguably two highest authorities in the field. Jasanoff and Hilgartner are internationally leading scholars in Science and Technology Studies and have done extensive research on the social dimensions and politics of biomedicine and biotechnology. In their conversation, they explained how they study not only the practices of knowledge production, in laboratories and elsewhere, but also how such practices both shape and are shaped by other institutions and practices. In short, their work attempts to make sense of science, and life science in particular, by asking "But what about life science? Can it make sense of life?". In order to answer that question, Jasanoff and Hilgartner explained, one has to realize that "sense" has several meanings. One concrete example that was discussed also in the subsequent Q&A session, was human infertility. Medical research has provided humanity with knowledge and technology – notably IVF techniques – to help overcome involuntary infertility. In that way, science makes (scientific and technical) sense of the condition. However, sometimes the scientific ideas also migrate into human culture and self-understanding, for instance by classifying infertility as a disease and thereby giving it connotations of pathology. This amounts to a medicalization that may suppress other ways of

making sense of life. The question is accordingly not so much if science can make sense of life, but rather when, and in which circumstances, it should do so.

Jasanoff's and Hilgartner's work is an important foundation for CCBIO's own work on the ethical and societal aspects of cancer biomarkers. As Lars A. Akslen, Director of CCBIO, stated: "This seminar was truly inspirational and provided some clues on how to reflect on what we do in a center like CCBIO."

The seminar was rounded off with interesting discussions and an engaging Q&A session, and informal social interactions over coffee and light food.

Startup seminar for Carina Strell, August 25. The Trond Mohn Foundation (TMS) awarded in 2022 Carina Strell a TMS starting grant for her project *Understanding Early Breast Cancer Evolution in Space and Time (EvoMaps)*. Flowers and smiles were in abundance when representatives from TMS, CCBIO, the Department of Clinical Medicine and the Medial Faculty welcomed Carina Strell to the University of Bergen August 25, by way of a seminar with speakers giving talks with direct relevance for Strell's field of research.

Strell has a long-term collaboration with the Akslen group at CCBIO. In her TMS-funded project, Strell aims to understand the biological mechanisms behind why some women experience recurrent or treatment resistant breast cancer 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. The overall aim of this project is to uncover and map new mechanisms of early breast cancer evolution.

Carina Strell gave the presentation *Tumor-Stroma Interactions Driving Progression and Therapy-Resistance of DCIS*, explaining how getting a better understanding of breast cancer evolution early on can improve treatment by identifying new therapeutical targets to overcome radio-resistance and establishing new biomarkers to reduce the current overtreatment. Using novel molecular tools for advanced tissue analysis, she 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. She explained how she will use the Hyperion Imaging System at CCBIO to investigate genotype-microenvironment interactions at the onset of invasive disease.

Two other speakers shed light on the importance of breast cancer research from different angles. **Therese Sørlie** (University of Oslo) gave the talk *Intrinsic subtypes and spatial heterogeneity in Ductal Carcinoma In Situ (DCIS)*, showing how this non-invasive form of breast cancer has increased dramatically during the last decades, especially after the introduction of mammography screening. Sørlie's talk covered her group's ongoing work on studying the molecular heterogeneity in DCIS and the relevance of the intrinsic subtypes of breast cancer in breast tumor progression. **Solveig Hofvind** (Cancer Registry of Norway) presented early detection of breast cancer in a screening and registry perspective, showing statistics on how breast cancer is the most frequent cancer type among women in the world, with an increased incidence for invasive breast cancer mainly for stage I. Survival from breast cancer has increased substantially during the last decades. Hofvind presented the BreastScreen Norway program, which aims to reduce breast cancer mortality by detecting the tumors at an early stage.

The CCBIO Director Lars A. Akslen finds it highly important to strengthen breast cancer research at the UiB and has been very impressed by Carina's work over the years and through his collaboration with her. He is convinced that her innovative approaches in the breast cancer field will continue to stimulate CCBIO's efforts.

CCBIO Mini Symposium "Treatment approaches for elderly/unfit patients with AML in the Nordic countries." November 9, 2022, CCBIO hosted a Mini Symposium in collaboration with the educational working group in the Nordic AML Group, on the topic *"Treatment approaches for elderly/unfit patients with AML in the Nordic countries"*, as a webinar shown in the auditorium Storsalen at the AHH building, Haukeland University Hospital campus. Meeting facilitator for the webinar was **Pia Ettala**, specialist in internal medicine and clinical hematology, Turku University Hospital and chairman for the Educational Working Group, with local introduction from **Irini Ktoridou-Valen** in Bjørn Tore Gjertsen's group, and local chairpersons **Pål Tore Bentsen** and **Anette Lodvir Hemsing**.

The outcomes for elderly/unfit patients with acute myeloid leukemia remain dismal due to limited treatment options. The aim of this webinar was to highlight the emerging treatment options and discuss Nordic practices for this challenging population. **Mika Kontro**, MD, PhD, consultant at Helsinki University Hospital, Finland, gave an overview of treatment of unfit AML patients in Finland, and **Gunnar Juliusson**, professor and consultant at Skaane University Hospital, Sweden presented the treatment of the elderly/unfit AML patients in Sweden. This was followed by case presentations, and a panel discussion by the panelists **Mika Kontro**, **Anders Dahm**, MD, PhD, consultant and associate professor, Akershus University Hospital, Norway, **Hans B. Ommen**, MD, PhD, consultant and associate professor, Aarhus University Hospital, Denmark, and **Martin Jädersten**, MD, PhD, consultant, Karolinska University Hospital, Sweden. ••

10TH CCBIO ANNUAL SYMPOSIUM 2022

The **10th CCBIO Annual Symposium** took place at Solstrand Hotel May 10 and 11, 2022, finally as an onsite event, attracting about 200 onsite and 60 online participants.

The symposium started with a highly inspirational keynote presentation by **Robert S. Langer**, founder of Moderna and considered the "Edison of Medicine". Langer shared generously from his vast experience, ranging from when he was a young scientist, through his first paper and first talk, the mentorship by Dr. Judah Folkman, the startup of his first company, overcoming skepticism and barriers and finally achieving great successes.

The symposium program was set up in order to give a broad focus to research topics relevant to cancer biomarkers. **Olli Kallioniemi**, director of the SciLifeLab and professor at the Karolinska Institute, presented real-time functional precision cancer medicine in acute myeloid leukemia, as opposed to DNA sequencing based efforts by the identification of oncogenic driver mutations. Pancreatic cancer was covered by **Malin Sund** from the University of Helsinki and Umeå University, as well as by **Daniel Öhlund** from Umeå University. **Carina Strell** presented early breast cancer and development of progression and therapy resistance, showing different models for cancer evolution. Breast cancer was also covered by **Christine Desmedt** from the Laboratory for Translational Breast Cancer Research (LTBCR), University of Leuven, who showed how correct diagnosis at the pathology level is crucial. Cancer surgery also needs to be precise, as showed by **Gooitzen van Dam**, professor of surgery, nuclear medicine and molecular imaging at the University of Groningen, as well as CEO & founder of TRACER. He showed their digestible drug delivery device, as well as intraoperative tumor-specific fluorescence imaging. **Sébastien Wälchli** showed interesting projects "from classic to modern CAR repertoire". He works at the Department of Cellular Therapy/Translational Research Unit at Oslo University Hospital, where he leads the development platforms for molecular biology of the T-cell receptor (TCR) and the Chimeric Antigen Receptor (CAR). **Srinivas Malladi** from the UT Southwestern Medical Center and the Harold C. Simmons Comprehensive Cancer Center showed important targetable dependencies of latent brain metastatic cells, and **Rolf Brekken** from UT Southwestern and a member of the CCBIO International Faculty reported on intriguing results of restoring sensitivity to immune checkpoint blockade through inhibition of AXL.

The last session of the symposium contained presentations from two excellent basic scientists addressing the issue of capturing the diversity of cancer in relevant experimental models for precision oncology. **Matthias Nees** from the University of Turku and the University of Lublin shared from his experience on "benchmarking" of some of the most widely used *ex vivo* tumor models, including patient-derived organoids and explants, tissue-engineered models, and organ-on-chip approaches. **Silvio Gutkind** from Moores Cancer Center, University of California, San Diego took us through the challenges of head and neck cancer and the elegant approach his lab was using by employing a comprehensive kinome assay and a syngeneic mouse model to discover new, more efficient multimodal immunotherapeutic approaches for this type of cancer.

Roger Strand chaired a slides free panel debate celebrating the output from the CCBIO ELSA team, the new book *Precision Oncology and Cancer Biomarkers: Issues at Stake and Matters of Concern*, by editors Anne Blanchard and Roger Strand. The panel debate, built around the ideas that are discussed in the book, allowed for an open discussion by the panelists **Marta Bertolaso**, professor of philosophy of science at the University Campus Bio-Medico of Rome (UCBM) and a member of the CCBIO International Faculty, CCBIO Researcher Anne Blanchard, **Dominique Chu**, lecturer in Computer Science at the University of Kent with a special interest in the philosophy of complex systems and biology, and **Bjørn Hofmann**, professor at the Norwegian University of Science and Technology at Gjøvik and an adjunct professor at the Centre for Medical Ethics at the University of Oslo.

The program also provided ample time for young researchers through 3-minute speed talks, a format that proved successful in last year's digital version of the symposium and now continued both live and online, and a poster session each day, with a total of 14 speed talks and 49 posters. Each day, the audience voted for best speed talk and poster.

The 2022 symposium enabled CCBIO as a whole and our guests and friends to finally meet in-person for the first time since 2019. This clearly gave the gathering an extra level of positive energy throughout. We feel confident that this will be the case also for CCBIO's 10-year anniversary celebration at the three-day **11th CCBIO Annual Symposium** at Solstrand May 8-10, 2023. ••

The 10th CCBIO Annual Symposium

May 10 - 11, 2022
at Solstrand Hotel & Bad












Centre for Cancer Biomarkers

10th CCBIO Annual Symposium 2022

May 10-11, 2022 Solstrand - Bergen Norway (on-site and online event)

DAY ONE — Tuesday May 10, 2022

09:45-10:00	**Welcome and Opening: Lars A. Akslen (Director of CCBIO)**
	Chair: Bjørn Tore Gjertsen
10:00-11:00	CCBIO Keynote Lecture Robert S. Langer: From a 1976 Nature paper to a 2020 mRNA vaccine: How overcoming skepticism and barriers led to new cancer treatments and the solution to a global health challenge
11:00-11:30	Olli Kallioniemi: Functional and data-driven precision medicine in acute myeloid leukemia
11:30-12:00	Malin Sund: Early detection of pancreatic cancer
12:00-12:30	Daniel Öhlund: Targeting tumor-stromal interactions in pancreatic cancer
12:30-14:30	**Lunch and poster session**
	Chair: Roger Strand
14:30-15:45	Imaginaries of Precision Oncology. Panel: Marta Bertolaso, Anne Blanchard, Dominique Chu, Bjørn Hofmann
15:45-16:30	**Coffee**
	Chair: Oddbjørn Straume
16:30-17:00	Carina Strell: Tumor-stroma interactions driving the progression and therapy resistance of DCIS
17:00-17:30	Christine Desmedt: Unraveling disease progression and treatment resistance in patients with lobular breast cancer
19:30	**Dinner**

DAY TWO — Wednesday May 11, 2022

09:00-09:45	Gooitzen van Dam: Clinical molecular imaging: a multidisciplinary tool in cancer treatment from drug development, image-guided surgery to cancer pathology
09:45-10:15	Sébastien Wälchli: From classic to modern CAR repertoire
10:15-10:45	**Coffee**
	Chair: Jim Lorens
10:45-11:15	Srinivas Malladi: Uncovering targetable vulnerabilities of breast cancer brain metastatic cells
11:15-11:45	Rolf Brekken: Restoring sensitivity to immune checkpoint blockade through inhibition of AXL
12:00-14:00	**Lunch and poster session**
	Chairs: Liv C. V. Thomsen, Line Bjørge
14:00-15:00	Speed presentations by young investigators
	Chair: Dana Costea
15:15-15:45	Matthias Nees: Automated tracking of tumor-stroma morphology in microtissues identifies targets within the tumor microenvironment for therapeutic intervention
15:45-16:15	Silvio Gutkind: Targeting the PIK3CA-mTOR network in head and neck cancer: New multimodal precision immunotherapies
16:15-16:30	Roger Strand: Closing remarks













14


































OTHER MEETINGS

While CCBIO is very satisfied with its annual symposium and seminar structure, we and our research groups also organize and contribute towards a range of other meetings and activities as shown by the below examples.

Symposium on tumor and tissue fibrosis June 9-10, 2022, in Bergen. This symposium was organized by **CCBIO PI Donald Gullberg**. In addition to the international collaborators Ritva Heljasvaara, Sergey Plutnikov, Roger Oria-Fernandez, Chris McCulloch, Tom Barker, Andreas Romaine, Ronen Schuster, Andrew Leask, Roya Navab, Humphrey Gardner and Erine Budi, CCBIO's Daniela Costea, Harsh Dongre and Stian Tornaas as well as Donald Gullberg himself, contributed with lectures. Topics discussed included fibroblasts, collagens XIII and XV in fibrosis, cytoskeleton protection by formin mDia1, mechano-transduction in cancer, the role of DDR1 in fibrosis, the matrix as a major driver and therapeutic target of fibrosis, hart fibrosis, mapping of fibroblast-macrophage interactions, targeting the microenvironment in fibrotic condition, CAF heterogeneity in squamous cell carcinoma and in drug-tolerant persisted non-small cell lung cancer tumor, stromal phenotypic markers and disease outcome in solid tumors, and development of integrin inhibitors to treat fibrotic disease. The symposium also included a demonstration of the Hyperion Imaging System at CCBIO.

Movie and panel discussion – "Of medicine and miracles", October 25 in Bergen. An event from the **Norwegian Biotechnology Advisory Board** (which is led by **CCBIO Associate PI Ole-Frithjof Norheim** and with **CCBIO alumnus Eirik Tranvåg**), and BIFF, Bergen International Movie Festival. BIFF showed the highly praised documentary *Of Medicine and Miracles*, which portrays immunologists and oncologist Carl June and his work to develop a cure for cancer, more specifically CAR-T immunotherapy. After the movie, there was a panel discussion (in Norwegian) at Kulturhuset.

SCANPATH - the Scandinavian Symposium on Translational Pathology, November 14-15, 2022. SCANPATH is a CCBIO-initiated annual network meeting for Scandinavian tumor pathologists and pre-clinical scientists with an interest in the prospects of next generation tissue profiling. The aim is to stimulate tissue-based studies of tumor mechanisms and biomarker mapping. SCANPATH was founded by CCBIO Director Lars A. Akslen and PI Arne Östman in 2016 (Bergen).

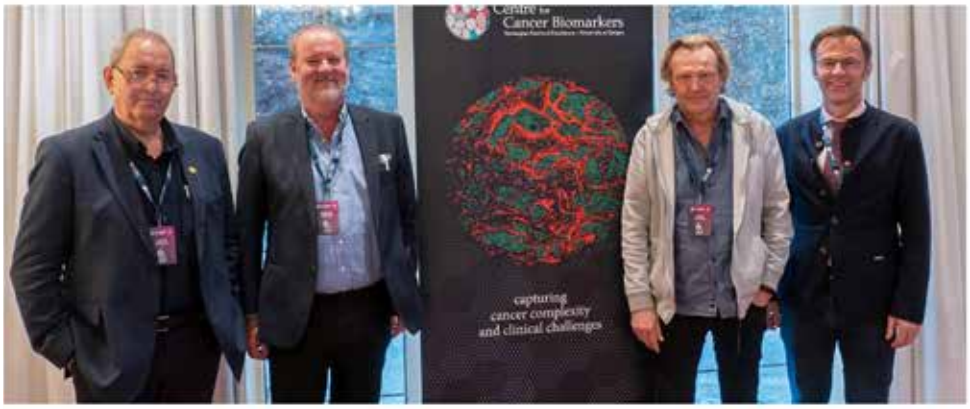
SCANPATH is by now a well-established annual forum. Since the first meeting in Bergen, Norway (2016), further meetings were held in Sigtuna, Sweden (2017), Gustavelund, Tuusula, Finland (2018), Solstrand, Bergen, Norway (2019), and Tylösand, Sweden, (2021). The 2020 event was cancelled due to the pandemic. In 2022, SCANPATH returned to Solstrand, Bergen, hosted by CCBIO. Top Scandinavian tumor pathologist and pre-clinical scientists came to present and discuss tissue-based studies of tumor mechanisms and biomarker mapping.

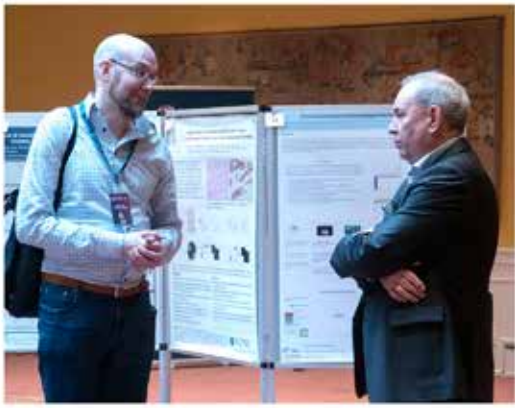
Over 100 participants – an all-time high for this meeting – enjoyed the beautiful surroundings at Solstrand and listened to 35 presentations, spanning from AI-based precision pathology to identification of tumor microenvironment cell subsets as prognostic factors in various tumors, and diving into discovery-based studies as well as more biomarker-oriented presentations. The potential of novel methodologies was indicated in a series of presentations, many of which relied on the Hyperion Imaging Mass Cytometry-system established at CCBIO. SCANPATH included scientists with various backgrounds, facilitating fruitful discussions and cross fertilization and starting new collaborations. The Posters and Prosecco session enabled young researchers to share and discuss their work with the conference participants. Three posters received awards, nominated by audience voting.

SCANPATH once again felt almost like a family gathering, with a friendly atmosphere and a "microenvironment" that facilitated cross-communication and networking between groups and scientists. This represents a key resource for the future. The 2023 meeting will be held in Finland. ••

6th Scanpath

November 14 - 15, 2022
at Solstrand Hotel & Bad





Centre for Cancer Biomarkers

6th SCANPATH Network Meeting | DAY ONE

Day 1: Monday – November 14, 2022

09:00-10:00	**Registration and coffee**
10:00-10:15	**Lars A. Akslen: Welcome and introduction**
	Chair: Arne Östman
10:15-10:45	Mattias Rantalainen: AI-based precision pathology – scalable solutions for cancer patient stratification and phenotyping
10:45-11:00	Marit Valla: AICAN: AI for automatic breast cancer segmentation
11:00-11:15	Mehrdad Rakaee: AI-based pathology predicts immunotherapy response in lung cancer
11:15-11:30	Stephanie Robertson: Stratipath – Realworld application of AI-based image analysis in pathology
11:30-11:45	Cecilia Lindskog Bergström: Transcriptomics and antibody-based proteomics for mapping single-cell profiles of human tissues in health and disease
11:45-12:00	Guttorm Haraldsen: Single cell genomics during drug treatment — a novel aspect of intelligent drug design
12:00-13:30	**Lunch**
	Chair: Marit Valla
13:30-14:00	Pernilla Wikström: Biological and clinical relevance of the transcriptomic-based prostate cancer metastasis subtypes MetA-C
14:00-14:15	Therese Sørlie: Spatial gene expression analysis reveal heterogeneity in HER2-enriched ductal carcinoma *in situ*
14:15-14:30	Lise Ingebriktsen: Age-related biomarkers in breast cancer
14:30-14:45	Helga Bergholtz: Canine mammary gland tumors - comparable molecular subtypes between dogs and humans
14:45-15:00	Anna Sæle: Loss of GATA3 expression associates with aggressive breast cancer, and predicts increased immunological responses
15:00-15:15	Dimitrios Kleftogiannis: Single-cell analysis of breast cancer by imaging mass cytometry
15:15-15:30	Company presentation by AH Diagnostics and Standard Biotools
15:30-16:00	**Coffee & Crosstalk**
	Chair: Carina Strell
16:00-16:15	Artur Mezheyeuski: Immune patterns across tumor types
16:15-16:30	Oscar Briem: Prognosis from tumor-infiltrating immune cells in advanced breast cancer
16:30-16:45	Hui Yu: Relevance of T-cell clonality in NSCLC
16:45-17:00	Amanda Lindberg: The role of active PDGFRb signaling in NSCLC
17:00-17:15	Roberta Lugano: CD93 in regulation of tumor vessel function
17:15-17:30	Company presentation by Miltenyi (Christian Garm)
17:30-17:45	Company presentation by Aiforia (Darshan Kumar)
18:30-19:30	**Posters & Prosecco**
19:30	**Dinner**

Day 2: Tuesday – November 15, 2022

Chair: Therese Sørlie

09:00-09:30	Teijo Pellinen: Identification of tumor microenvironment cell subsets as prognostic factors in renal cell carcinoma
09:30-09:45	Camilla T. Ekanger: Human organotypic airway and lung models to study danger signaling mediated immunosurveillance
09:45-10:00	Agnete S. T. Engelsen: The impact of phenotypic plasticity on the tumor immune interface
10:00-10:15	Ole Vidhammer Bjørnstad: Proteomic changes induced in co-cultured breast cancer spheroids by neural progenitor cells
10:15-10:30	Carina Strell: Spatial profiling of tumor heterogeneity in breast cancer
10:30-11:00	**Coffee & Crosstalk**

Chair: Patrick Micke

11:00-11:15	Anna Klemm: Support on image analysis by the BioImage Informatics Facility, Sweden
11:15-11:30	Fredrik Nysjö: Image analysis and visualization for multiplexed image data
11:30-11:45	Martina Bosic: Deep skin annotation in Human Protein Atlas - a resource for cellular and functional classification of skin proteome
11:45-12:00	Hilde Lien: High dimensional analysis of tumor heterogeneity in recurrent and nonrecurrent FIGO I endometrial carcinomas using imaging mass cytometry
12:00-13:30	**Lunch**

Chair: Agnete Engelsen

13:30-13:45	Joshua Cumming: Cancer-associated fibroblast heterogeneity in pancreatic cancer
13:45-14:00	Linglong Huang: Discovery and spatial characterization of mesenchymal cell subsets in human colon cancer
14:00-14:15	Harsh Dongre: Decoding fibroblast heterogeneity by using imaging mass cytometry
14:15-14:30	Helena Järemo: Effects of microRNA-23c and -4328 overexpression in metastatic prostate cancer cells and tumor microenvironment
14:30-14:45	Natalie Andersson: Phylogenetic analysis of pediatric tumors
14:45-15:00	Martin E. Johansson: Clear cell renal cell carcinoma. Histological heterogeneity follows from metabolic heterogeneity
15:00-15:15	Arne Östman: Closing remarks

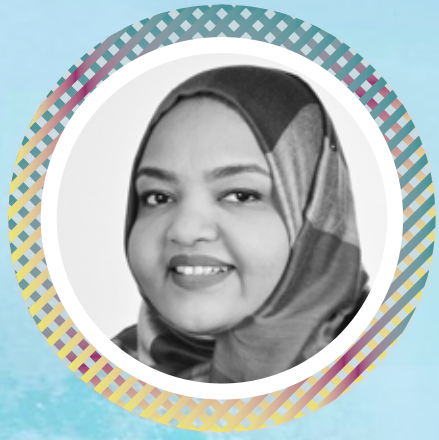
DISSERTATIONS

Our PhD candidates' doctoral defenses are 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 2022, 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 2022 (chronological order):

CALUM LEITCH
"Identification and development of small molecule therapies for the treatment of acute myeloid leukaemia." Supervisors: Professor Bjørn Tore Gjertsen and PhD Vibeke Andresen. Defense date: February 11, 2022.



NUHA MOHAMMED GAAFAR MOHAMMED
"Prognostic biomarkers and tumour immune microenvironment characterization in oral squamous cell carcinoma." Supervisors: Professor Daniela Elena Costea, Professor Anne Chr. Johannessen, PhD Elisabeth Sivy Nginamau and PhD Tarig Osman. Defense date: March 25, 2022.

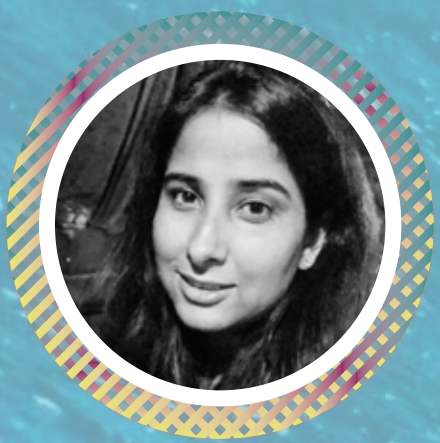
SUSHMA PANDEY DHAKAL
"Prognostic roles of proliferation- and differentiation-related proteins in oral leukoplakia and oral squamous cell carcinoma." Supervisors: Associate Professor Dipak Sapkota (UiO) and Professor Daniela Elena Costea. Collaboration project between UiB and University of Oslo (UiO). Defense date: February 18, 2022.

YING CHEN
"The tumor microenvironment in breast cancer: A study of stromal elastosis, tumor immune cells, vascular invasion, and the relation to detection mode." Supervisors: Professor Lars A. Akslen, Associate Professor Elisabeth Wik and PhD Tor Audun Klingen. Defense date: April 8, 2022.

DISSERTATIONS

HEGE FREDRIKSEN BERG
"Organoid models and novel biomarkers for improved treatment of endometrial cancer." Supervisors: Professor Camilla Krakstad and PhD Erling Høivik. Defense date: April 22, 2022.

SILJE KJØLLE
"Tumor microenvironment in breast cancer progression. A mass spectrometry-based proteomics study for biomarker discovery and validation." Supervisors: Professor Lars A. Akslen, PhD Kenneth Finne and PhD Heidrun Vethe. Defense date: August 30, 2022.



RIDHIMA DAS
"Novel Methods and Sources for Regeneration of Oral Mucosa." Supervisors: Professor Daniela Elena Costea, Professor Anne Christine Johannessen, Professor Mihaela-Roxana Cimpan and PhD Salwa Suliman. Defense date: June 16, 2022.

HILDEGUNN SIV AASE
"Digital Breast Tomosynthesis - the future screening tool for breast cancer?" Supervisors: Professor Solveig Hofvind and Professor Ingfrid S. Haldorsen. Defense date: October 31, 2022.

CECILIE ASKELAND
"Biomarkers of aggressive breast cancer with emphasis on tumor-stroma crosstalk." Supervisors: Professor Lars A. Akslen, Associate Professor Elisabeth Wik and Professor Ingunn Stefansson. Defense date: December 9, 2022.

SUSHIL DHAKAL
"AXL targeting to enhance tumor Type 1 interferon response and potentiate chemo-immunotherapy." Supervisors: Professor James Lorens and Associate Professor Niels Aarsæther. Defense date: December 16, 2022.

JIYEON KANG
"Improving economic evaluation and decision-making for oncology drugs using real-world data." Collaboration project between UiB and the London School of Hygiene and Tropical Medicine. Supervisors: Professor John Cairns and Associate Professor Alec Miners. Defense date: December 13, 2022.

CCBIO BOOKS

CCBIO has published three books through coordinated research activities and cross-field collaboration.

The first, published in April 2017, entitled *Cancer Biomarkers: Ethics, Economics and Society*, is edited by Roger Strand and Anne Blanchard (Bremer) from the CCBIO ELSA group, with contributions from several of the CCBIO teams.

This book is intended to stimulate reflections on how we design and perform biomarker research. On top of basic and clinical projects, bringing in these additional topics could have the power to intensify our reflection on own activities. This goes to the core of the RRI-concept, i.e., to perform responsible research and innovation.

In more detail, the book focuses on cancer care undergoing a shift from a "'one-size-fits all" approach to more personalized medicine. One way of personalizing cancer treatments is through biomarkers: molecules or biochemical changes found in the patient's tissues and body fluids. The book reflects upon the promise of cancer biomarkers and asks questions such as: How may the complexity of cancer biology impede the robustness of biomarkers in the clinic? How should one draw the line between the various sub-groups of patients for personalized treatment? How can one evaluate the cost-effectiveness and fairness of personalized cancer treatments? By bringing together authors from the fields of science and technology studies, medical ethics and philosophy, health economics and oncology, the book aims to give a critical yet accessible overview of some of the key social, ethical and economic issues that surround cancer biomarkers.

Bruce Zetter, Charles Nowiszewski Professor of Cancer Biology in the Department of Surgery, Harvard Medical School, commented:

"The book should be required reading for oncologists, medical students, graduate students and especially for those who make policy decisions regarding the use and reimbursement of cancer biomarkers."

The book can be obtained e.g. from Amazon.

The same year, in August 2017, CCBIO with editors Lars A. Akslen and Randolph S. Watnick published *Biomarkers of the Tumor Microenvironment - Basic Studies and Practical Applications*, at Springer Publishing. Several CCBIO investigators and affiliated professors contributed.

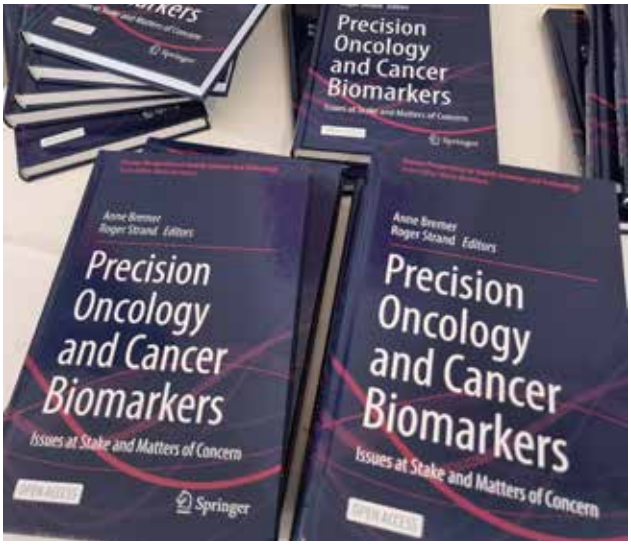
In 2022, this book was published in a new and extended format as a Springer textbook: Lars A. Akslen and Randolph S. Watnick (eds): *Biomarkers of the Tumor Microenvironment*. The considerably enlarged second edition deals with the most important aspects of the tumor microenvironment, providing an in-depth analysis of the interactions that take place between normal and malignant cell types. It provides a rather exhaustive scrutiny of the phenotypes and organization of various tissue components, decoding the roles enacted by vascular cells, stromal fibroblasts, inflammatory cells, immune cells, and neural cells within the tumor microenvironment. The book provides insight into the clinical relevance of important signaling systems. The advent of new technologies is also discussed, with a reflection on how these methods are being applied for the discovery and validation of new biomarkers towards the optimization of clinical trials.

Biomarkers of the Tumor Microenvironment is aimed at cancer researchers from various backgrounds and research pathologists in the cancer field, in particular those using advanced morphology techniques and models focusing on crosstalk between different cell types in tumors.

This textbook can be obtained through Springer, and is also available in open access, with more than 24 000 accesses by January 2023.

2022 also saw the publication of the interdisciplinary research anthology *"Precision Oncology and Cancer Biomarkers: Issues at Stake and Matters of Concern"*, edited by Anne Blanchard and Roger Strand and with 17 contributors from the CCBIO ELSA network. The book's key focus is the interdisciplinary analysis of the sociotechnical imaginaries of personalized and precision cancer medicine.

This volume reflects on matters of social and ethical concern raised in the daily practices of those working in and around precision oncology. Each chapter addresses the experiences, concerns, and issues at stake for people who work in settings where precision oncology is practiced, enacted, imagined or discussed. It subsequently discusses and analyses bioethical dilemmas, scientific challenges and economic trade-offs, the need for new policies, further technological innovation, social work, as well as phenomenological research.



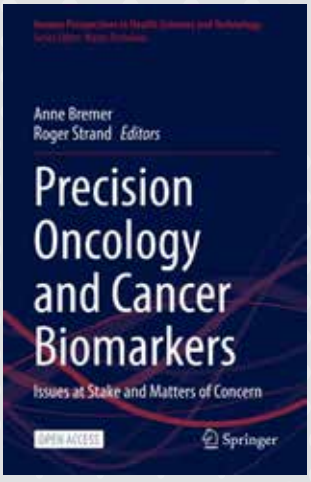
This volume takes a broad actor-centered perspective as, whenever cancer is present, the range of actors with issues at stake appears almost unlimited. This perspective and approach open the possibility for further in-depth and diverse questions, posed by the actors themselves, such as: How are cancer researchers navigating biological uncertainties? How do clinicians and policymakers address ethical dilemmas around prioritization of care? What are the patients' experiences with, and hopes for precision oncology? How do policymakers and entrepreneurs envisage precision oncology? These questions are of great interest to a broad audience, including cancer researchers, oncologists, policymakers, medical ethicists and philosophers, social scientists, patients and health economists.

The new edition can be obtained through Springer, and is also available in open access, with more than 19 000 accesses by January 2023. ••

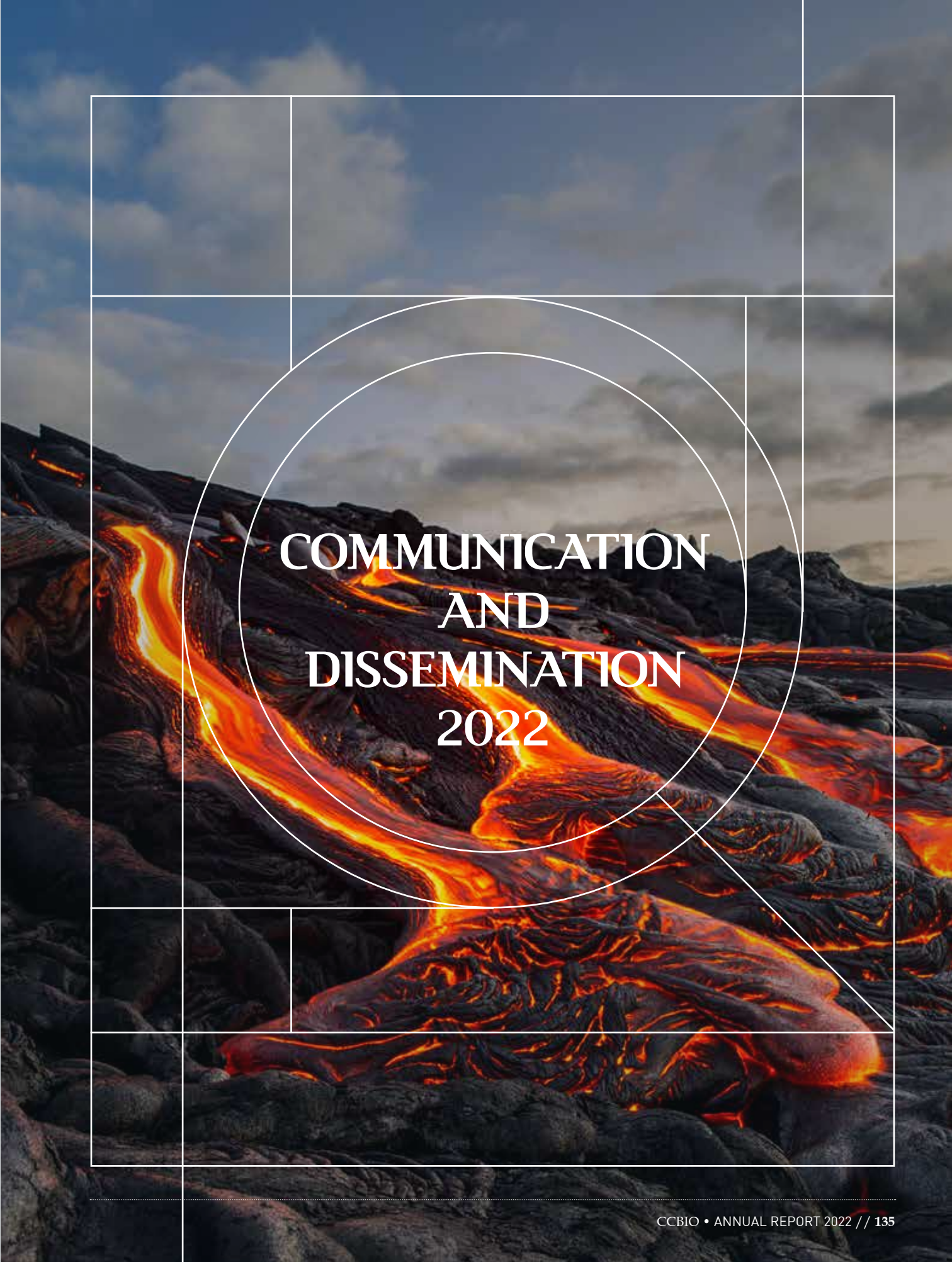
Cancer Biomarkers: Ethics, Economics and Society

Biomarkers of the Tumor Microenvironment

Precision Oncology and Cancer Biomarkers: Issues at Stake and Matters of Concern




Haukeland



COMMUNICATION AND DISSEMINATION 2022

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.

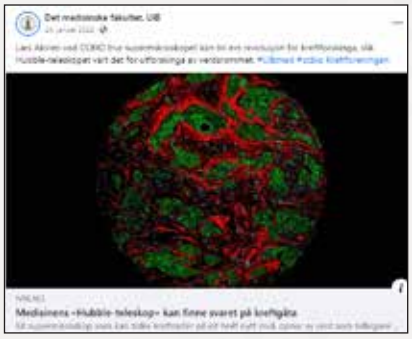
CCBIO issues a newsletter at regular intervals (6 issues per year) and keeps its webpages updated, presenting news stories from our research community, and ensuring that our numerous open events are well advertised. Also, social media has grown to be a tool and connector for governmental organizations, businesses, and individual users. We promote our researchers, scientific findings, happenings, media appearances and behind-the-scenes glimpses via the Faculty of Medicine's Facebook and Twitter accounts and encourage 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 2022:

FACEBOOK entry on the annual ceremony for the Trond Mohn Foundation, celebrating their grants through the year, among other a starting grant to Carina Strell to establish a breast cancer research group at CCBIO. The event also featured a presentation of the Bergen Centre for Ethics and Priority Setting – BCEPS, led by CCBIO PI Ole-Frithjof Norheim, which recently has been awarded status as a Centre of Excellence.

FACEBOOK entry on financial support, here from the Norwegian Cancer Society and 8 mill. NOK to a project by CCBIO PI James Lorens.

FACEBOOK entry on the awarding of the SpareBank 1 SMN Talent Award of 50.000 NOK to Medical Student Amalie Fagerli Tegnander in the Akslen and Wik groups for her combination of medical studies with breast cancer research.



FACEBOOK entry about CCBIO's Hyperion Imaging System and its potential to revolutionize cancer research.

FACEBOOK entry on CCBIO events, here the CCBIO/Neuro-SysMed course CCBIONEUR910, Patient and Public Involvement in Medical and Health Research.

FACEBOOK entry on CCBIO's major event through the year, the Annual Symposium 2022 at Solstrand.

FACEBOOK entry on Bob Langer's visit to CCBIO's Annual Symposium 2022.

TWITTER entry on a joint event between CCBIO and the Holberg Prize: *"Can science make sense of life?"* with the 2022 Holberg Prize winner Sheila Jasanoff in conversation with Stephen Hilgartner.

TWITTER entry on one of the many international conferences attended by CCBIO groups, including poster presentations, here by PhD Candidate Kari Wagner-Larsen from the Krakstad group at the RSNA 2022 in Chicago.

TWITTER entry on interviews with CCBIO scientists, here on the current topic women's health and an interview with CCBIO Associate Investigator and Research School leader Elisabeth Wik.

CCBIO also 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. Henriette stages stories that take place inside the body, more specifically within the individual cell, and introduce that teeny-tiny biology not visible even in the microscope. A perceived total lack of common decency among cancer cells invites to relatable stories that can explain cancer to a child. Henriette is a molecular biologist with experience in age-dependent cancer. Having also studied acting she tells the story of the wondrous biology of cells with great skill. In 2022, 484 pupils in the Bergen area got to experience the tumor microenvironment on stage through 8 performances in schools during the year and 8 performances at the children's summer camp at the VilVite science exhibition in Bergen.

MEDIA APPEARANCES 2022

DECEMBER 20, 2022 – ONKOLOGISK TIDSSKRIFT
"Lavdose cellegift før stamcelletransplantasjon viser like gode resultater som høydose mot r/r AML" - Pål Tore Bentsen

DECEMBER 20, 2022 – KREFTFORENINGEN
"Vanner ville vyer med millioner" - Carina Strell

DECEMBER 19, 2022 – DAGBLADET
"Ny kreftmedisin vekker oppsikt" - Line Bjørge

DECEMBER 13, 2022 – HEALTHTALK
"Pasienter med akutt myelogen leukemi kan leve lenger med ny behandlingsform"- Bjørn Tore Gjertsen

NOVEMBER 12, 2022 – KHRONO
"Til vanleg forskar han på brystkreft. Men onsdag kveld er det oboen som er i fokus" - Manuel Carrasco

NOVEMBER 9, 2022 – NRK
"Forskere forbauset: Kvinne (36) overlever aggressiv kreft gang etter gang" - CCBIO Hyperion photo used

NOVEMBER 4, 2022 – DAGBLADET
"Fikk skrekkbeskjed: - Trodde det var covid"
- Bjørn Tore Gjertsen

NOVEMBER 2, 2022 – KREFTFORENINGEN.NO
"186 millioner til livsviktig forskning" - Jim Lorens

OCTOBER 31, 2022 – HEALTHTALK
"Hun utvikler miniversjoner av bukhinnen for å bedre forstå hvordan eggstokkreft utvikler seg og kan behandles" - Christiane Helgestad Gjerde

OCTOBER 29, 2022 – HEALTHTALK
"Fant ulik immunrespons hos pasienter med eggstokkreft som ble behandlet med to immunterapier" - Luka Tandaric

OCTOBER 27, 2022 – HEALTHTALK
"ESGO 2022: – PARP hemmere er det største medisinske gjennombruddet de siste 30 årene – nå kommer også immunterapi" - Line Bjørge

OCTOBER 24, 2022 – NORSKE KVINNERS SANITETSFORENING
"3D-printer mini-svulster for å finne medisin mot vulvakreft" - Rammah Mustafa Elnour, Harsh Dongre and Rezan Erman

OCTOBER 13, 2022 – NRK TV
"Holbergsamtalen 2022" - Roger Strand

MEDIA APPEARANCES

SEPTEMBER 26, 2022 – UIB NEWS
"Two new Centres of Excellence to the University of Bergen"
- Ole Frithjof Norheim

SEPTEMBER 23, 2022 – KHRONO
"Tre på rad for Moser-miljøet. 5 av 9 sentre til Universitetet i Oslo" - Ole Frithjof Norheim

SEPTEMBER 23, 2022 – FORSKNINGSRÅDET
"1,4 milliarder kroner til ni nye sentre for fremragende forskning" - Ole Frithjof Norheim

SEPTEMBER 19, 2022 – ONKOLOGISK TIDSSKRIFT
"Lederen for den nordiske AML-gruppen: Vi har store ambisjoner" - Bjørn Tore Gjertsen

SEPTEMBER 11, 2022 – HEALTHTALK
"ESMO-studie: - En del av pasientene med eggstokkreft som fikk olaparib ble kurert" - Line Bjørge

AUGUST 1, 2022 – DAGENS MEDISIN
"Det er tillatt å være saklig, Kristiansen"
- Eirik Joakim Tranvåg and Ole Frithjof Norheim


'Please do not erase': A treasured whiteboard at Boston Children's Hospital has not been touched for 15 years

JULY 28, 2022 – BOSTON GLOBE
"'Please do not erase': A treasured whiteboard at Boston Children's Hospital has not been touched for 15 years"
- Lars A. Akslen

JULY 7, 2022 – VI.NO
"Paracetamol kan påvirke kreftbehandling negativt"
- Oddbjørn Straume

JULY 7, 2022 – DAGENS MEDISIN
"Beslutningsforum følger føringer som er satt"
- Eirik Joakim Tranvåg


Bergens Tidende

Paracet kan svekke effekten av immunterapi hos kreftpasienter

– Vi må kanskje være forsiktige med bruk av Paracet til disse pasientene, sier Haukeland-overlege.

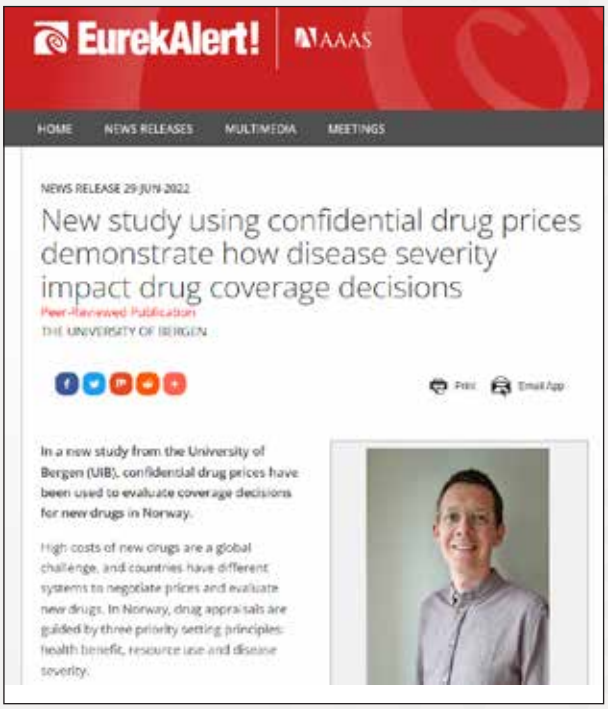
JULY 6, 2022 – BERGENS TIDENDE
"Paracet kan svekke effekten av immunterapi hos kreftpasienter" - Oddbjørn Straume

JULY 5, 2022 – DAGENS MEDISIN
"Studie reiser spørsmål om paracetamol og immunterapi"
- Oddbjørn Straume


Beslutningsforum betaler meir for å behandle alvorlege tilstandar

I ein ny studie frå Universitetet i Bergen (UiB) er hemmelege legemiddelpanar nytta til å vise korleis sjukdommen sin alvorsgrad påverkar betalingsviljen for nye legemiddel i Noreg.

JULY 1, 2022 – UIB NEWS
"Beslutningsforum betaler meir for å behandle alvorlege tilstandar" - Eirik Joakim Tranvåg


EurekAlert! | AAAS

HOME NEWS RELEASES MULTIMEDIA MEETINGS

NEWS RELEASE 29-JUN-2022

New study using confidential drug prices demonstrate how disease severity impact drug coverage decisions

Peer-Reviewed Publication

THE UNIVERSITY OF BERGEN

In a new study from the University of Bergen (UiB), confidential drug prices have been used to evaluate coverage decisions for new drugs in Norway.

High costs of new drugs are a global challenge, and countries have different systems to negotiate prices and evaluate new drugs. In Norway, drug appraisals are guided by three priority setting principles: health benefit, resource use and disease severity.

JUNE 29, 2022 – EUREKALERT!
"New study using confidential drug prices demonstrate how disease severity impact drug coverage decisions"
- Eirik Joakim Tranvåg

JUNE 29, 2022 – PÅ HØYDEN
"Høg kvalitet på innovasjonsidear"
- Harsh Dongre and Line Bjørge

JUNE 29, 2022 – DAGENS MEDISIN
"Bør Norge bruke mer penger på helsetjenester?"
- Ole Frithjof Norheim

JUNE 22, 2022 – UIB NEWS
"Sju forskere om kjønnsforskjeller og helse"
- Elisabeth Wik

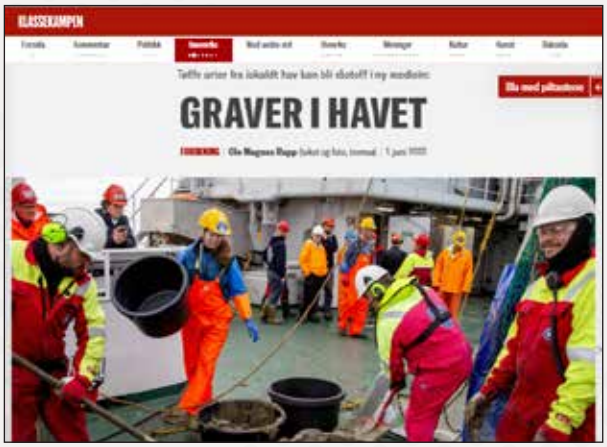
MEDIA APPEARANCES


Aftenposten

Grunnforskning kan ikke settes på vent

JUNE 14, 2022 – AFTENPOSTEN
"Grunnforskning kan ikke settes på vent" - Lars A. Akslen

JUNE 3, 2022 – MORGENBLADET
"Vi må anerkjenne det politiske i forskningen"
- Roger Strand


KLASSEKAMPEN

GRAVER I HAVET

JUNE 1, 2022 – KLASSEKAMPEN
"Graver i havet" - Bjørn Tore Gjertsen


DAGENS Medisin

100 millioner kroner til klinisk forskning

MAY 27, 2022 – DAGENS MEDISIN
"100 millioner kroner til klinisk forskning"
- Bjørn Tore Gjertsen

MAY 25, 2022 – HELSE VEST
"100 millionar til klinisk forsking: Fire av fem prosjekt er frå Vestlandet" - Bjørn Tore Gjertsen

MAY 13, 2022 – SPRINGER LINK
"Reply to comment on 'Demonstrating the value of cancer biomarkers at the population' " - Ana Luís and Kelly Seo

MAY 6, 2022 – NETTAVISEN.NO
"Eggstokkreft er kjent som en «silent killer»: Slik vet du om du bør reagere" - Line Bjørge

MAY 2, 2022 – HEALTHTALK
"Dyrker kreftceller i mininatyrlunger"
- Agnete Engelsen and Camilla Ekanger

MAY 1, 2022 – UIB NEWS
"Ny styreleder i AI-konsortium" - Inge Jonassen

APRIL 25, 2022 – VG
"Derfor øker kreftrisikoen" – Therese Sørlie

MARCH 30, 2022 – SPRINGER LINK
"Demonstrating the value of cancer biomarkers at the population level" – Ana Luís and Kelly Seo

MARCH 29, 2022 – FORSKNING.NO
"Slik driver forskere med «etterretning» for å forstå kreft"
- Lars A. Akslen

MARCH 22, 2022 – TIDSSKRIFT FOR DEN NORSKE LEGEFORENING
"Forskning og patologi hånd i hånd" - Lars A. Akslen

MEDIA APPEARANCES


The Harvard Crimson

Harvard Kennedy School Professor Sheila Jasanoff '64 Awarded Prestigious Holberg Prize

Sheila Jasanoff, a professor of science and technology studies at the Harvard Kennedy School, was awarded the Holberg Prize for 2022. By Sheila Jasanoff / Jean Baptiste Paris via Wikimedia Commons

By Miles J. Herszenhorn, Crimson Staff Writer

MARCH 21, 2022 – THE HARVARD CRIMSON
"Harvard Kennedy School Professor Sheila Jasanoff '64 Awarded Prestigious Holberg Prize" - Roger Strand

MARCH 15, 2022 – PÅ HØYDEN
"Tverrfaglig forskning skal flytte forskningsfronten"
- Emmet McCormack

MARCH 14, 2022 – AFTENPOSTEN VITEN
"Hvorfor blir vi enige om noe som helst?" - Roger Strand

MARCH 1, 2022 – BUSINESS WIRE
"Papyrus Therapeutics Announces Formation of Scientific Advisory Board" - James Lorens

FEBRUARY 26, 2022 – NY TEKNIKK
"UiB koordinerer innsatsen på kunstig intelligens"
- CCBIO

FEBRUARY 21, 2022 – DAGENS MEDISIN
"Venter en bølge av nye dyre behandlinger"
- Bjørn Tore Gjertsen


SciTechDaily

BIOLOGY CHEMISTRY EARTH HEALTH PHYSICS SCIENCE SPACE TECHNOLO

HOME HEALTH NEWS

Obesity Is Linked With Cancer – Now We Finally Know Why

Cancer is caused by genetic changes that break down normal constraints on cell growth. It is known that obesity and overweight increases the risk of developing cancer, but the question until now has been why? Now, researchers at University of Bergen have demonstrated that lipids associated with obesity make cancer cells more aggressive and likely to form actual tumors.

JANUARY 23, 2022 – SCITECHDAILY
"Obesity is linked with cancer – now we finally know why" - James Lorens, Noelly Madeleine, Stacey D'Mello Peters, Cara Ellen Wogsland and Sturla Magnus Grøndal


NRK

Supermikroskop kan finne svaret på kreftgåta

Eit supermikroskop som kan tolke kreftceller på eit heilt nytt nivå, opnar ei verd som tidlegare var skjult for forskarane. Mikroskopet kan vise vegen til løysinga av kreftgåta, trur kreftforskar.

JANUARY 21, 2022 – NRK.NO
"Supermikroskop kan finne svaret på kreftgåta" – Lars A. Akslen, Kenneth Finne and Heidrun Vethe

JANUARY 20, 2022 – NRK1 VESTLANDSREVYEN
"Supermikroskop skal brukes i kreftforskningen"
- Lars A. Akslen, Kenneth Finne and Heidrun Vethe

JANUARY 20, 2022 – NRK1 KVELDSNYTT
"Tror på gjennombrudd" - Lars A. Akslen, Kenneth Finne and Heidrun Vethe

JANUARY 20, 2022 – NRK1 ROGALANDSNYTT
"Supermikroskop skal brukes i kreftforskning"
- Lars A. Akslen, Kenneth Finne and Heidrun Vethe

JANUARY 15, 2022 – FORSKNING.NO
"1 av 5 som dør av kreft, har fedme. Nå vet forskere mer om hvorfor" - Therese Sørlie

MINI BIOGRAPHIES

PhD Candidates, Postdocs and Researchers 2022

ASKELAND, CECILIE
MD from the University of Bergen and a senior pathologist at the Department of Pathology, Haukeland University Hospital. She was PhD candidate in the Akslen group until her doctoral defense in December 2022, 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. Her doctoral work was titled "Biomarkers of aggressive breast cancer with emphasis on tumor-stroma crosstalk."

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.

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
PhD from the University of Bergen in 2022 on preclinical modeling and biomarkers in endometrial cancer. She is currently a postdoctoral fellow in the Krakstad group where her main focus is to study carboplatin resistance in endometrial cancer.

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 nerve involvement.

BLANCHARD, ANNE
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. Blanchard 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, published by Springer in 2022: *"Precision Oncology and Cancer Biomarkers: Issues at stake and matters of concern"*.

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 on 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.

CASTELLS MARIN, ORIOL
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 treatment responses in acute myeloid leukemia clinical trials.

CHEN, YING
MD, pathologist and currently medical director at Fürst Medical Laboratory (Oslo). She completed her PhD in April 2022 with the thesis "Tumor microenvironment in breast cancer – a study of stromal elastosis, tumor immune cells, vascular invasion and the relation to detection method," supervised by Lars A. Akslen, Tor-Audun Klingen, and Elisabeth Wik. Her PhD project focused on breast cancer stroma with the aim to identify the interplay between tumor-infiltrating lymphocytes, vascular invasion and stromal elastosis. She is still a member of the Akslen group.

DAS, RIDHIMA
Certified dental surgeon from India with an MS in experimental oral pathology from Queen Mary University London, UK. She was until her doctoral defense in June 2022 a PhD candidate in the Costea group with the PhD project "Novel Methods and Sources for Regeneration of Oral Mucosa". The aim of the project was to explore the possibility of producing oral mucosa in the laboratory, among other things using so-called "induced pluripotent stem cells – iPSCs". Das used stem cells both in cell culture and in animal models to develop oral mucosa. This gives hope that in the future, such methods can be used clinically to replace lost tissue during surgery.

D'MELLO, STACEY
PhD in molecular medicine from the University of Auckland. She was in 2022 a postdoc in the Lorens group, working on tumor cell plasticity in malignant melanoma and its role in therapy resistance with a particular focus on AXL receptor kinase mechanisms.

DE MONTLAUR, CONSTANCE DE VILLARDI
PhD in animal physiology from the University of Paris and currently a researcher in the McCormack group. She is working on a project related to precision medicine and development of immunotherapy in childhood cancer. Her research focuses on the development of novel preclinical models for solid and hematological pediatric cancers for the evaluation of repurposing approved drugs and the investigation of immunotherapies.

DHAKAL, SUSHIL
MS in biomedical sciences from the University of Bergen. He was until his doctoral defense in December 2022 a PhD candidate in the Lorens group, with the PhD project "AXL targeting to enhance tumor type 1 interferon response and potentiate chemoimmunotherapy". In this work, Dhakal investigated how the AXL receptor inhibits the interferon response in tumor cells. The work uncovers how cell signals from AXL block the tumor cell activation of interferon and the anti-tumor immune response. Overall, the results show a new treatment principle with a potential to improve the efficacy of immunotherapy for cancer patients.

DHAKAL, SUSHMA PANDEY
MDS in oral medicine and radiology from MCODS, Manipal University, Karnataka, India, and BDS from BPKIHS, Nepal. She was a PhD candidate at the University of Oslo, jointly with the Costea group, until her doctoral defense in February 2022. Her research project "Prognostic roles of proliferation- and differentiation-related proteins in oral leukoplakia and oral squamous cell carcinoma" aimed 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.

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 medical cell biology from the University of Bergen. She is currently pursuing her PhD in the Signaling Targeted Therapy and PreCOS groups of Gjertsen and McCormack. Her research focuses on clonal selection and heterogeneity in acute myeloid leukemia (AML). To mimic clonal architecture of myeloid malignancies she has explored modeling AML using patient derived xenografts and a novel humanized bone marrow stem cell derived scaffold, focusing on identifying potential biomarkers and 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.

EKANGER, CAMILLA TVEDT
MS in biomedical sciences from the University of Bergen and currently a PhD candidate in the Engelsen group. Her PhD project focuses on developing and characterizing organoids and explant models of normal lung tissue and non-small cell lung cancer (NSCLC) tissues. She is also currently coordinating CCBIO's seminars.

ESPEDAL, HEIDI
PhD in neuro-oncology from the University of Bergen. She was from late 2018 to August 2022 a postdoc in the Krakstad group, with a focus on functional imaging of endometrial cancer mouse models.

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

FOSSE, VIBEKE
MS in veterinary companion animal oncology and veterinary surgeon, and currently a PhD candidate in the McCormack and Bjørge groups. Her project is on the development of targeted fluorescence image-guided surgery, with a focus on using clinically relevant animal models for translation. In particular, she is developing a comparative oncology approach, using pets with cancer as models for development of therapies for human disease.

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.

GOLD, ROSE MENG
A computational biologist from the United States with a background in computer science and biomedical engineering. Currently, she is a researcher in the Krakstad group where she analyzes sequencing data for endometrial cancer. Her main project is to examine pre- and post-chemotherapy whole-genome sequencing samples to explore the effects of carboplatin on the cancer genome.

GRØNDAL, STURLA MAGNUS
MS in nanoscience from the University of Bergen and 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, he is 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. For the 2022/2023 terms, she is coordinating the CCBIO Junior Scientist Symposia together with Vladan Milosevic.

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 (AML) 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.

HJELMELAND, MARTA ESPEVOLD
MS in biomedicine from the University of Bergen, and currently a PhD candidate in the Krakstad group. Her main research focus is on pre-clinical models and identifying new treatment strategies for endometrial cancer patients. She is currently located in Boston where she is working in Rameen Beroukhim's lab at Dana-Farber and Broad Institute of MIT and Harvard University.

HUA, YAPING
PhD from the University of Bergen in 2020 and currently a postdoc in Kalland's group. She works on the discovery of novel potential anti-cancer compounds and the identification of corresponding molecular targets in human prostate cancer cells. This innovative project strategy combines cancer cell cryoimmunotherapy with exclusively available panels of biologically active compounds that are isolated from medicinal herbs and plants (phytochemicals).

HUGDAHL, EMILIA
MD, and 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 IHC.

HUMLEVIK, RASMUS OLAI COLLETT
MD from Riga Stradiņš University, Latvia and currently a PhD candidate in the Wik and Akslen groups with Elisabeth Wik as main supervisor. His project is focused on age-dependent differences in immuno-angiogenic responses in breast cancer.

HØIVIK, ERLING
PhD in molecular biology from the University of Bergen. He is currently a researcher in the Wik and Akslen groups, working on breast cancer with a particular focus on younger patients. He uses multiangled "omics"-approaches to explore and characterize new biomarkers to improve treatment for these patients.

INGEBRIKTSEN, LISE MARTINE
MS in biomedicine from the University of Tromsø. She is currently a PhD candidate in the Wik and Akslen 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.

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.

KANG, JIYEON
PharmD and MS in Global Health from the London School of Economics and Political Science. She completed her PhD project "Improving economic evaluation and decision-making for oncology drugs using real-world data" in December 2022 at the London School of Hygiene and Tropical Medicine, supervised by John Cairns. She starts her short-term postdoc in Cairns and Strand groups in spring 2023, aiming to further develop and disseminate her research effectively.

KJØLLE, SILJE
MS in molecular biology from the University of Bergen. She completed her PhD in August 2022 with the thesis "Tumor microenvironment in breast cancer progression. A mass spectrometry-based proteomics study for biomarker discovery and validation." Supervisors were Professor Lars A. Akslen, PhD Kenneth Finne and PhD Heidrun Vethe. Currently she is a researcher in the Akslen group. Her research is focused on hypoxia patterns in breast cancer. The project aims to explore the hypoxia response at the proteomic level and effects of hypoxia on the tumor microenvironment and processes involved in tumor progression.

KLEFTOGIANNIS, DIMITRIOS
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.

KTORIDOU-VALEN, IRINI
MD from the University of Semmelweis, Budapest, working as a consultant medical oncologist at the Haukeland University Hospital. Currently, she is a PhD candidate in the Gjertsen group. Her project focuses on the repurposing of known drugs for the treatment of refractory acute myeloid leukemia with the aim to explore and determine biomarkers of early response.

LEITCH, CALUM
MS in molecular and cellular biology from the University of Glasgow. Until February 2022, he was a PhD candidate in the Gjertsen group until the completion of his PhD project "Identification and development of small molecule therapies for the treatment of acute myeloid leukemia". His project focused 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. He continues as a researcher in McCormack's group.

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 and is currently a PhD candidate in the Krakstad group where she is using imaging mass cytometry to investigate tumor heterogeneity and biomarkers in endometrial cancer, also in collaboration with the Akslen group.

LINDBERG, AMANDA
MS in biomedicine from Uppsala University, and currently a PhD candidate in the Strell group, working from the Uppsala University site. Her research is focused on spatial mapping of signaling pathway activation in non-small cell lung cancer (NSCLC), and how to use this knowledge to identify novel therapeutic targets as well as biomarkers.

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 was until the summer of 2022 a postdoc in the Lorens group, working on imaging mass cytometry and high dimensional analysis of the tumor microenvironment.

LURA, NJÅL GJERDE
MD with background in internal medicine and radiology. He is currently working on a PhD project in the Krakstad group, studying 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.

MESQUITA, ÂNGELA
MS in molecular genetics and 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 of novel 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.

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 on integrin α11β1 as a regulator of the interplay between tumor and stromal cells.

MICONGWE, MOSES ISYAGI
BDS and MMed in Pathology from Makerere University, Uganda, and a PhD candidate enrolled at Makerere University. Currently, he is on a 1-year NORPART PhD exchange in Costea's group at CCBIO. His research interests focus on diagnostic interval enablers and barriers to early diagnosis and management of oral cavity cancer.

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 chemoresistant and immune resistant phenotypes 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. For the 2022-2023 terms, he is coordinating the CCBIO Junior Scientist Symposia together with Mari K. Halle.

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

MOHAMED, NUHA
MS in periodontics from the University of Khartoum. From August 2016 to her doctoral defense in March 2022, she was a PhD candidate in the Costea group. Her PhD project "Prognostic biomarkers and tumor immune microenvironment characterization in oral squamous cell carcinoma" focused on prognostic biomarkers in oral cancer patients with specific focus on the inflammatory host reaction and its correlation to survival of patients from Sudan.

MOTZFELDT, INGA KRISTINE FLAATEN
MS in biomedicine from the University of Bergen, and currently 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 was in 2022 a researcher in the Lorens group. His research project focused on the role of the receptor tyrosine kinase AXL in the context of cancer.

MUSIIME, MOSES
PhD in biomedicine from the University of Bergen, 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 Gullberg group, focusing on the analysis of the cooperative roles of integrin α11 and syndecan-4 in fibroblasts using the fibrotic mouse heart as a model system.

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 establishment of patient derived organoid (PDO) models which can be used to predict drug response in vulva cancer by using mass cytometry (CyTOF).

OWIBINGIRE, SIRA STANSLAUS
Senior lecturer and oral maxillofacial surgeon at Muhimbili University of Health and Allied Sciences (MUHAS) in Tanzania. He is a part time PhD candidate at MUHAS focusing on oral and oropharyngeal cancer, more specifically profile of risk factors and quality of life among clinically suspected oral and oropharyngeal squamous cell carcinoma patients. He is currently a NORPART exchange PhD student in Costea's group.

PAPYAN, ROBERT
MD, Resident in Pathology at Yerevan State Medical University in Armenia. During his stay as a guest researcher in the Costea group in 2022, he conducted a study of multiple biomarkers in oral squamous cell carcinoma patients from Armenia with the view of further analyzing their prognostic value.

PARAJULI, HIMALAYA
PhD from the University of Bergen focusing on integrin α11 in oral carcinogenesis. Having worked on melanoma brain metastases in a different lab, he is now a guest researcher in the Costea group, working on oral carcinogenesis.

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.

RANA, NEHA
MS in biochemistry from India. She is since 2018 a PhD candidate in the Gjertsen and Mustafa 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 IL7 isoforms from the Karolinska Institute. He started working in the Gjertsen group as a postdoc in 2015, investigating p53 isoforms in acute myeloid leukemia. Currently he is a researcher in the same group, investigating novel small molecule CSF1R and FLT3 inhibitors in acute myeloid leukemia.

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

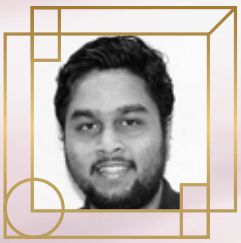
RØSLAND, GRO VATNE
PhD in molecular cell biology from the University of Bergen. Her PhD project focused on mechanisms of glioblastoma progression, with an emphasis on stem cell markers and the epidermal growth factor system. In 2021-2022 she was a researcher in the Lorens group, where she worked on AXL-mediated 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.

SCHIZA, AGLAIA
MD, PhD from Uppsala University, and senior oncologist as well as postdoc in the Strell group, working from the Uppsala University site. She has a strong research interest in neuroimmunology and how this interaction can impact breast cancer initiation, progression and response to immunotherapy. Schiza further focuses on the repurposing of beta-adrenergic blocking agents and neurokinin 1 (NK1) receptor antagonists in cancer therapy.

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 with a special interest in markers related to stress response. She is a co-investigator in a clinical trial for patients with metastatic melanoma.

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



SIRAJI, MUNTEQUA ISHTIAQ
MS in biomedical sciences from the University of Bergen and currently a PhD candidate in the Lorens group, on 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.

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 using mass cytometry and humanized mouse models.

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 and Gjertsen groups. 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.

THURFJELL, VIKTORIA
MD from Umeå University and currently a surgical pathologist subspecializing in breast pathology and a PhD candidate in the Strell group, working from the Uppsala University site. Her PhD project focuses on spatial characterization of immune response in ductal carcinoma *in situ* (DCIS). She aims to understand the regulatory mechanisms behind distinct immune infiltration patterns and how those are connected to radiotherapy response and disease progression.

TISLEVOLL, BENEDICTE SJO
MD from the University of Bergen. She is until her doctoral defense in January 2023 a PhD candidate in the Gjertsen group, with the PhD project "Single-cell protein profiling in early therapy response evaluation of acute myeloid leukemia by mass cytometry". Her work focuses 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 at the Department of Gynecology and Obstetrics, Stavanger University Hospital, and currently a PhD candidate in the Bjørge group. Her focus is to identify biomarkers in ovarian cancer with a special attention to the surgical management of the disease.

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 tissues.

TVEITARÅS, MARIA KATHRINE
MS in biomedicine and MD from the University of Bergen. She completed her PhD in January 2023, with Linda Stuhr and Rolf Reed as supervisors. Her PhD project focused on breast cancer metastasis, hypoxia, and the effect of hyperbaric oxygen treatment on targeting tumor hypoxia.

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.

WAGNER-LARSEN, KARI STRØNO
MD and currently 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.

ZELTZ, CÉDRIC
PhD in molecular and cellular biology from the University of Reims Champagne-Ardenne, France. He is currently a researcher in the Gullberg group. For over a decade, his research was essentially based on the interactions between cells and the extracellular matrix and on the determination of biomarkers and potential therapeutic targets in tissue and tumor fibrosis. His current project focuses on new integrin alpha11 mouse models for stroma targeting.

AASE, HILDEGUNN SIV
MD who completed her PhD in October 2022 in the Krakstad group with Solveig Hofvind (Norwegian Cancer Registry) as her main supervisor. Her PhD project focused on digital breast tomosynthesis (3D-mammography) in breast cancer screening, detection rates, reading times, breast density and mammographic features, comparing digital mammography (2D) and digital breast tomosynthesis. She is a radiologist and head of the Breast Centre in Haukeland University Hospital.

LIST OF PUBLICATIONS 2022

CCBIO - LIST OF PUBLICATIONS

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

Lellahi SM, Azeem W, Hua Y, Gabriel B, Paulsen Rye K, Reikvam H, Kalland KH. GM-CSF, Flt3-L and IL-4 affect viability and function of conventional dendritic cell types 1 and 2. *Front Immunol.* 2023 Jan 12;13:1058963. doi: 10.3389/fimmu.2022.1058963. PMID: 36713392; PMCID: PMC9880532

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CCBIO INFOGRAPHICS 2022

FACTS AND FIGURES 2022

PERFORMANCE INDICATORS	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	TOTAL
PUBLICATIONS	76	71	77	85	94	81	79	79	126	123	891
COMPLETED PHDS	5	6	3	10	12	9	8	15	8	11	87
EXTERNAL FUNDING MNOK	7.2	21.9	22.5	36.0	34.0	32.1	26.7	30.0	26.9	34	271
MEDIA APPEARENCES	39	11	32	31	54	40	68	54	54	54	437

CCBIO's scientific production continued on a high level in 2022. We expect a rise in 2023 as the last round of CoE financed PhDs, postdocs and researchers publish their results. As expected throughout 2022, the pandemic finally let up its grip on most of our activities. As a direct consequence, CCBIO was again able to use its funds to the best possible effect, resulting in the consumption of external funding increasing to 34 MNOK, constituting 39.6% of total funds used in 2022. 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.

GENDER DISTRIBUTION
(HEADCOUNT)

MALE
FEMALE

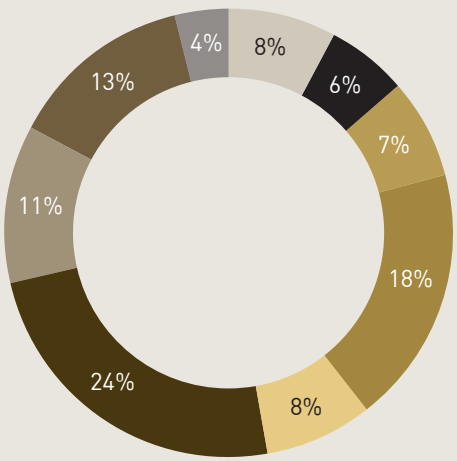
39%
61%

TOTAL: 218 PERSONS

Among the 218 persons involved in CCBIO, a stable majority are women, and of PhD candidates and postdocs, about 60% are female. Among senior scientific staff, the female share is steadily increasing year by year and currently 54%. CCBIO's active recruitment of excellent female staff during its second CoE-period has further increased the female part of its principal- and associate investigators from 27% to 35% in 2021-22. CCBIO undertakes no gender based affirmative action and recruitment of faculty is done purely on merit, and among more junior staff and future group leaders also on perceived potential. Looking back over the years, it is clear that the pool of female talent is such that merit-based recruitment is sufficient to gradually improve the gender balance in CCBIO's top tire.

CCBIO STAFF OVERVIEW
(HEADCOUNT)

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

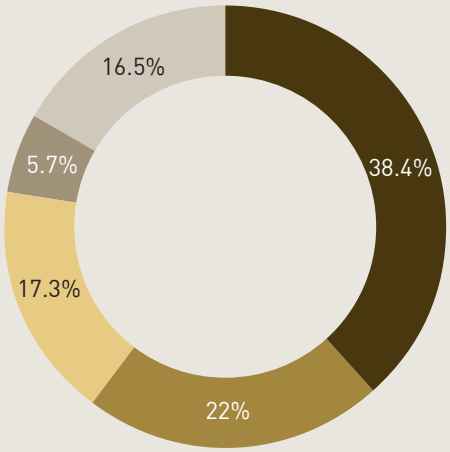


TOTAL: 218 PERSONS

CCBIO has a balanced composition of junior- and senior researchers, and support staff. To strengthen the ground for major breakthroughs and high-level publications, the center focuses on prolonging and developing the projects of top tire PhD candidates and postdocs. CCBIO has continued to recruit younger, predominantly female, investigators as full- and associate PIs. Through the CCBIO Masterclass program, a second batch of selected younger researchers currently receive targeted teaching and training to prepare them to become CCBIO's future group leaders. CCBIO's international network of 14 adjunct professors and researchers continue to ensure excellent access to high-level collaboration, advice, and tuition for CCBIO's researchers.

FUNDING
(FUNDS USED IN 2022)

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

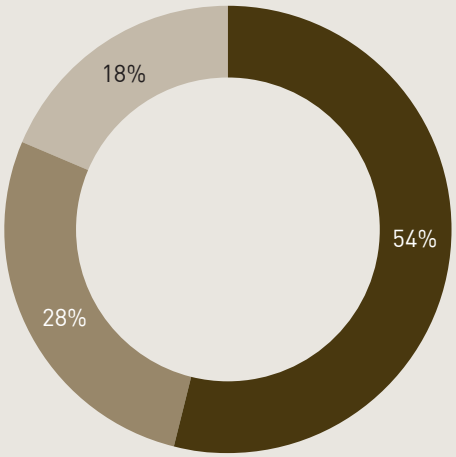


TOTAL: 85.9 MILL NOK

The pandemic-related shutdown of laboratories and consumables was gradually reversed throughout 2022. The increased level of activity is reflected in the 85,9 MNOK used, up from 76 MNOK in 2021. The consumption of external funds increased in absolute terms, from 26.4 MNOK to 34 MNOK, constituting 39.6% of funds used in 2022. CCBIO's external funding is well above twice the budgeted amount and illustrates a high success rate with funding agencies.

INTERNATIONALIZATION
(STAFF COUNTRY OF ORIGIN)

- NORWAY
- OTHER WESTERN COUNTRIES
- AFRICA & ASIA

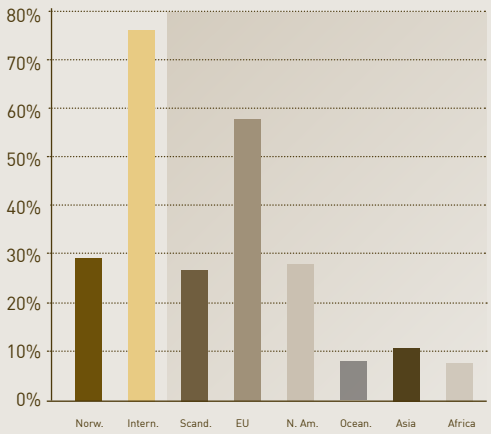


TOTAL: 218 PERSONS

Of CCBIO's overall staff, 46% have other citizenships than Norwegian, and 71% of its postdocs and 47% of PhD candidates originate from outside of Norway. Of CCBIO's international PhDs, two thirds originate from Asia and Africa. Among CCBIO's senior researchers, 44% are foreign nationals. CCBIO is a truly international Center of Excellence.

INTERNATIONALIZATION
(CO-AUTHORSHIPS)

- NORWAY OUTSIDE BERGEN
- INTERNATIONAL, OVER ALL
- SCANDINAVIA
- EUROPE
- NORTH AMERICA
- OCEANIA
- ASIA
- AFRICA

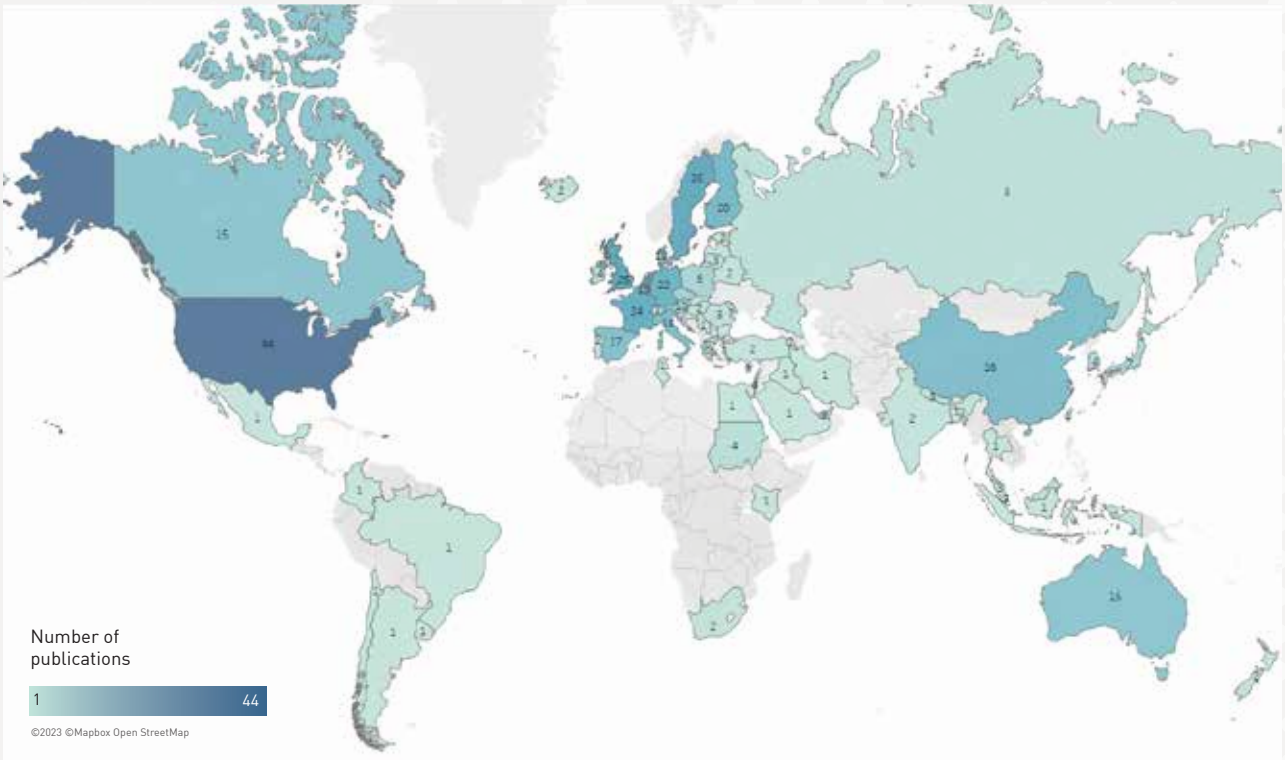


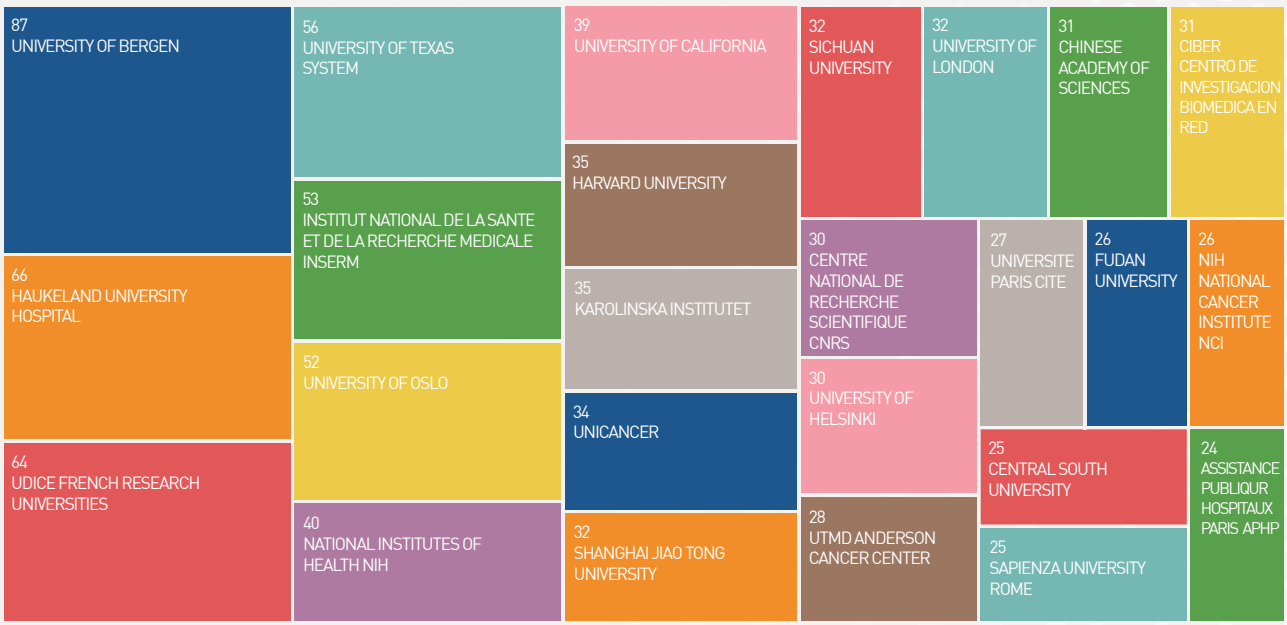
CCBIO's research continues to become increasingly internationalized through publication-based networks. The share of publications with co-authorships with researchers from other Norwegian universities decreased from 35% in 2020 to 29% in 2022, and solely Bergen-based publications now stand at a mere 9%. CCBIO's stronger international networks on the other hand generate an increasing number of publications with co-authors with their affiliation at international institutions, rising gradually from 58% in 2019 to 76% in 2021 and remaining stable throughout 2022. Further, the subdivision of international co-authorships into six regions (grayed out color) demonstrates that CCBIO collaborates with institutions from all major regions worldwide. If we then add up these six columns, we reach 140%. By comparing this total with the 76% in the "international aggregate"-category, we can conclude that the average international CCBIO publication in 2022 had co-authors from two regions, being truly multilateral. If then considering the rise from 122% in 2021 to 140% in 2022, we can discern a clear tendency of CCBIO's international research collaboration both widening and deepening as the center's CoE period draws to a close.

BIBLIOMETRICS

The figures reflect bibliometric analyses of CCBIO's medical PIs publications based on data from 2020-2022. The map focuses on the number of publications with co-authorships from each country. Every publication is counted once, regardless of the number of co-authors from the same country.

The area diagram at the bottom includes the number of publications with one or more citations of a CCBIO publication from each institution. Both the map and area diagram reflect CCBIO's strong international network and collaborations.





CCBIO ARCHIVE

Key elements in the history of CCBIO are well documented on our website (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.

Falch Lecture with Bob Langer (Video)

Bob Langer at the CCBIO Annual Symposium

It takes a village to run an online course

CCBIO Website

CCBIO in a Nutshell (video)

News Archive

The Hyperion Imaging System

The Laser Microdissection System

Want to book a performance?

Newsletters

Annual Reports

Opinions

Annual Symposia

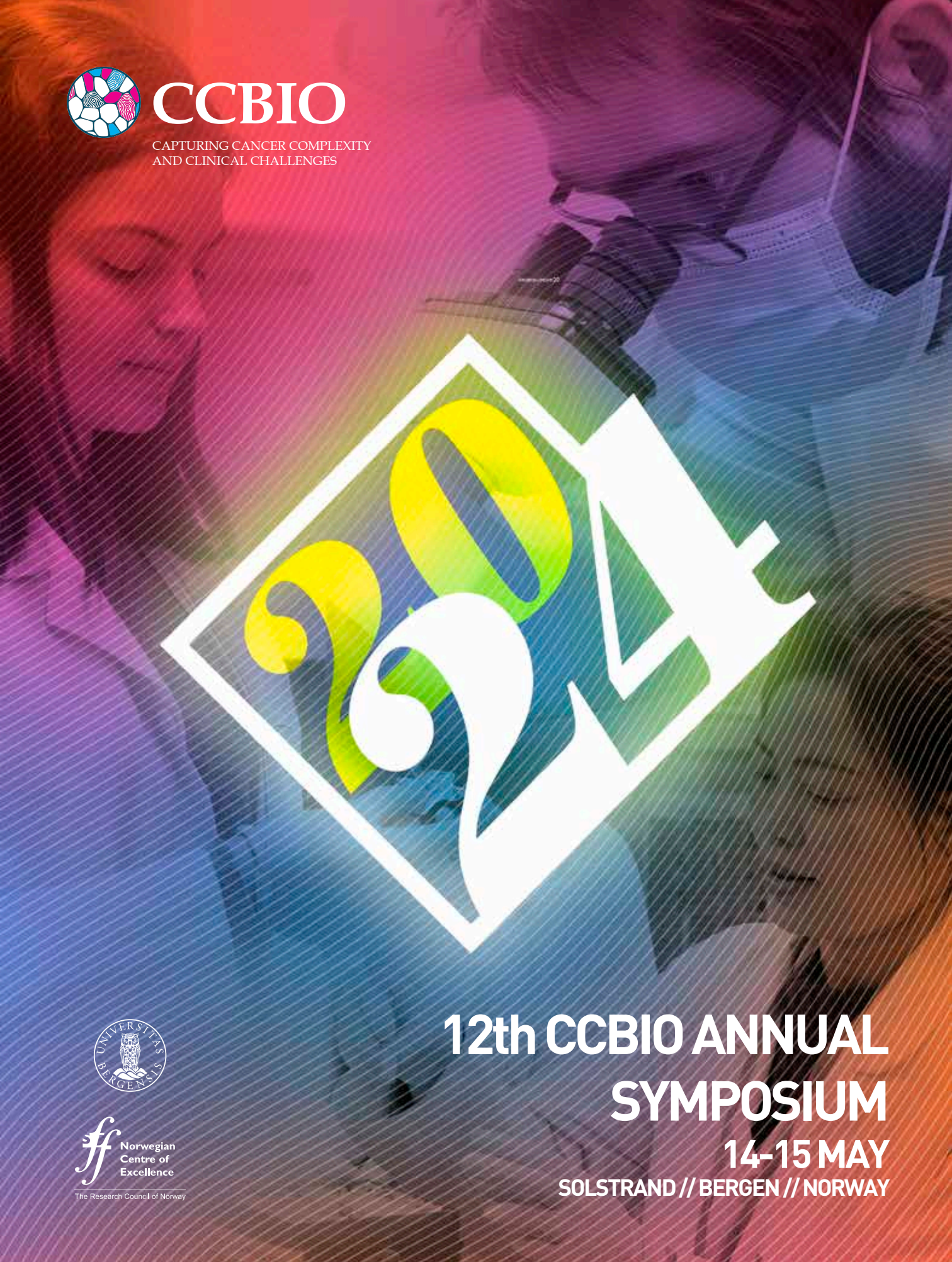
Upcoming CCBIO Symposium

Comments from Bruce R. Zetter

CCBIO Research School

The 2022 Holberg Prize Interview
(Jasanoff and Strand) (video)

Special Seminar by CCBIO and the Holberg Prize
Holberg Laureate, Sheila Jasanoff and Stephen Hilgartner



CCBIO

CAPTURING CANCER COMPLEXITY
AND CLINICAL CHALLENGES

2024

12th CCBIO ANNUAL SYMPOSIUM

14-15 MAY

SOLSTRAND // BERGEN // NORWAY

UNIVERSITAS BERGENSIS

Norwegian Centre of Excellence

The Research Council of Norway

LIST OF PERSONNEL AT CCBIO 2022

NAME	POSITION	ACADEMIC TITLE	GROUP
Akslen, Lars A.	Professor, Director	MD, PhD	Akslen
Aljiafiri, Asia	Master student		Costea
Alvarez Rivas, Carla	Guest postdoc	DDS, PhD	Costea
Amant, Frédéric	Adjunct professor	MD, PhD	CCBIO
Andresen, Vibeke	Senior researcher	MS, PhD	Gjertsen
Ardawatia, Vandana	Senior engineer	PhD	Akslen
Arnal, Emmanuelle Lucie	Master student		Engelsen
Arnes, Jarle Birger	Associated researcher	MD, PhD	Akslen
Askeland, Cecilie	PhD candidate	MD	Akslen
Azeem, Waqas	Senior engineer	MS, PhD	Kalland
Aziz, Sura Muhammed	Associated researcher	MD, PhD	Akslen
Bakke, Ragnhild Maukon	Stud.Med. (Medical Student Research Program)		Kalland
Baysal, Eylem	PhD candidate	MS	Costea
Benjaminsen, Susanne	Staff engineer	MS	McCormack
Bentsen, Pål Tore	PhD candidate	MD	Gjertsen
Berg, Hege Fredriksen	Postdoc	MS	Krakstad
Beroukhim, Rameen	Adjunct researcher	MD, PhD	CCBIO
Bertolaso, Marta	Adjunct professor	PhD	CCBIO/Strand
Bjørge, Line	Professor, Co-Director	MD, PhD, MBA	Bjørge
Bjørnstad, Ole Vidhammer	PhD candidate	MS	Akslen
Blanchard, Anne	Researcher	MA, PhD	Strand
Bougnaud, Sébastien	Associated researcher	MS, PhD	Lorens
Bourdon, Jean-Christophe	Adjunct researcher	MS, PhD	CCBIO
Bozickovic, Olivera	Staff engineer	MS, PhD	Krakstad
Bredin, Hanna	Stud.Med. (Medical Student Research Program)		Krakstad
Brekken, Rolf	Adjunct professor	MD, PhD	CCBIO
Børretzen, Astrid	Associated researcher	MD, PhD	Akslen
Cairns, John	Adjunct professor	MA, MPhil	Cairns
Carrasco, Manuel	Researcher	PhD	Akslen
Castells, Oriol	PhD candidate	MS	Gjertsen
Chen, Ying	Associated researcher	MD, PhD	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	Researcher	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
Dongre, Harsh	Postdoc	NanoMS, PhD	Costea/Bjørge
Dowling, Tara Helen	PhD candidate	MS	Gjertsen/McCormack
Dugstad, Jenny Margrethe	Technician	MS	Krakstad
Dybvik, Julie	PhD candidate	MD	Krakstad
Edelmann, Reidunn Jetne	Accociate professor	MD, PhD	Akslen
Ehsani, Rezvan	Postdoc	PhD	Jonassen/Akslen
Eide, Agnes Jørgensen	Stud.Med. (Medical Student Research Program)		Krakstad
Ekanger, Camilla Tvedt	PhD candidate	MS	Engelsen
Eldevik, Kristine Fasmer	PhD candidate	MS	Krakstad
Enge, Elisabeth	Study nurse		Krakstad/Bjørge
Engelsen, Agnete	Senior researcher	MS, PhD	Akslen/Lorens/Engelsen
Espedal, Heidi	Postdoc	MS, PhD	Krakstad
Fandalyuk, Zinayida	Staff engineer, lab manager	MS	McCormack
Finne, Kenneth	Senior engineer	PhD	Akslen
Fjeldstad, Karoline	Stud.Med.		Costea
Flatekvål, Helene Midtun	Head engineer	MS	Krakstad
Forsse, David	Consultant	MD, PhD	Krakstad
Fosse, Vibeke	PhD candidate, veterinarian	DVM	McCormack/Bjørge
Fromreide, Siren	Chief engineer	MS	Costea
Gabra, Hani	Adjunct professor	MD, PhD	CCBIO
Gabriel, Benjamin	Researcher	PhD	Kalland
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	MD, PhD	Gjertsen
Gold, Rose Meng	Researcher, computional scientist		Krakstad
Grigorian, André	Master student		Gullberg

NAME	POSITION	ACADEMIC TITLE	GROUP
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
Guttormsen, Maren Sofie Faldalen	Master student		Engelsen
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
Han, Jianhua	Head Engineer	PhD	Lorens
Hanif, Md Abu	Master student		Gjertsen
Harkestad, Kjetil	Senior executive officer		Administration
Hekmati, Neda	Lab manager		Strell
Hellberg, Louise	Pre-PhD candidate		Strell
Hellesøy, Monica	Researcher	MS, PhD	Gjertsen
Hernandez, Inni Merete Offerdal	Senior Executive Officer		Administration
Hjelmeland, Marta Espevold	PhD candidate	MS	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	Stud.Med. (Medical Student Research Program)		Akslen/Wik
Humlevik, Rasmus Olai Collett	PhD candidate	MD	Wik/Akslen
Høgås, Mildrid Bønes	Senior executive officer		Administration
Høivik, Erling André	Researcher	MS, PhD	Krakstad/Wik
Ingebriktsen, Lise Martine	PhD candidate	MS	Akslen/Wik
Jebsen, Nina Louise	Associate professor	MD, PhD	Gjertsen
Johannessen, Anne Christine	Professor	MD, DDS, PhD	Costea
Jonassen, Inge	Professor	MS, PhD	Jonassen
Kaliyugarasan, Satheshkuma	PhD candidate	MS	Krakstad
Kalland, Karl-Henning	Professor	MD, PhD	Kalland
Kalvenes, Mai Britt	Senior engineer	PhD	Akslen/Costea
Kang, Jiyeon	PhD candidate	MS	Cairns
Kimo, Magnus	Stud.Med.		Costea
Kjølle, Silje	Researcher	PhD	Akslen
Kleftogiannis, Dimitrios	Postdoc	PhD	Jonassen/Akslen
Kleinmanns, Katrin	Postdoc	PhD	McCormack/Bjørge
Klingen, Tor Audun	Associated researcher	MD, PhD	Akslen
Knutsvik, Gøril	Associated researcher	MD, PhD	Akslen
Kopperud, Reidun	Senior engineer	MS, PhD	Gjertsen/Straume
Krakstad, Camilla	Professor	MS, PhD	Krakstad
Ktoridou-Valen, Irini	PhD candidate	MD	Gjertsen
Kusche-Gullberg, Marion	Professor	MS, PhD	Gullberg
Kvamme, Amalie Bark	Stud.Med. (Medical Student Research Program)		Wik
LaBarge, Mark	Adjunct professor	MS, PhD	CCBIO
Le, Minh Thu	Study nurse		Bjørge
Leitch, Calum	Researcher	PhD	McCormack
Lellahi, Seyed Mohammad	Postdoc	PhD	Kalland
Lien, Hilde Eide	PhD candidate	MS	Krakstad
Lindberg, Amanda	PhD candidate	MS	Strell
Lindholm, Stein Rune	Research technician		Technical support
Litlekalsøy, Jorunn	Guest researcher	MS, PhD	Costea
Lode, Martine Rott	Master student		McCormack
Lorens, James B.	Professor	MS, PhD	Lorens
Lotsberg, Maria Lie	Postdoc	MS, PhD	Lorens
Lu, Ning	Senior engineer	MS, PhD	Lorens/Gullberg
Lura, Njål Gjerde	PhD candidate	MD	Krakstad
Lyngstad, Jenny	Stud.Med. (Medical Student Research Program)		Krakstad
Løken, Geir Olav	Administrative leader	MA	Administration
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
Micongwe, Moses Isiagy	PhD candidate	BDS, Mmed	Costea

NAME	POSITION	ACADEMIC TITLE	GROUP
Mills, Ian	Adjunct professor	MS, PhD	CCBIO
Milosevic, Vladan	Researcher	MD, PhD	Akslen
Mohamed, Hassan Abdel Raof-Ali	PhD candidate	DDS	Costea
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	MS	Costea/Bjørge
Myrvold, Madeleine	Stud.Med. (Medical Student Research Program)		Krakstad
Neppelberg, Evelyn	Adjunct associate professor	DDS, PhD	Costea
Nguyen, Rebecca	Lab technician		Gjertsen/Kalland
Nilsen, Irmelin Wilhelmsen	Guest researcher	M.Phil.	Strand
Norheim, Ole Frithjof	Professor	MD, PhD	Norheim
Olsen, Kristin Watnedal	Master student		Gjertsen
Omsland, Maria	Assistant professor	MS, PhD	Gjertsen
Owibingire, Sira Stanslaus	PhD candidate	MD	Costea
Pantel, Klaus	Adjunct professor	MD, PhD	CCBIO
Papyan, Robert	Guest researcher	MD	Costea
Parajuli, Himalaya	Postdoc	DDS, PhD	Costea
Peters, Stacey Ann D'Mello	Postdoc	PhD	Lorens
Pilskog, Martin	Guest researcher	MD, PhD	Straume
Poleo, Emilia Wold	Master student		Gjertsen
Pollard, Jeffrey	Adjunct professor	MS, PhD	CCBIO
Popa, Mihaela Lucia	Veterinarian	DVM	McCormack
Rajthala, Saroj	PhD candidate	MS	Costea
Ramnefjell, Maria	Associate professor	MD, PhD	Akslen
Rana, Neha	PhD candidate	MS	Gjertsen
Rane, Lalit Shirish	Researcher	MS, PhD	Gjertsen
Rausch, Jana Maria	Master student		Gullberg
Rayford, Austin	PhD candidate	MS	Lorens/Engelsen
Reed, Rolf K.	Professor	MD, PhD	CCBIO
Røsland, Gro Vatne	Researcher	MS, PhD	Lorens
Safont, Mireia Mayoral	Staff engineer		McCormack
Salvesen, Gerd Signe	Staff engineer		Reed
Sand, Louise Bergsjø	PhD candidate	MS	McCormack
Schiza, Aglaia	Postdoc	MD, PhD	Strell
Schuster, Cornelia	Postdoc	MD, PhD	Akslen/Straume
Sefland, Øystein	PhD candidate	MD	Gjertsen
Siraji, Muntequa Ishtiaq	PhD candidate	MS	Lorens
Siyam, Diana	Dental student (Medical Student Research Program)		Costea
Sletta, Kristine	PhD candidate	MS	Gjertsen
Smeland, Hilde Ytre-Hauge	Associated researcher	MS, PhD	Akslen
Solheim, Håkon Simen Haraldsøn	Senior executive officer	MA	Administration
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	Associate professor	PhD	Strell
Stuhr, Linda	Professor	MS, PhD	Reed
Suliman, Salwa	Senior researcher	DDS, PhD	Costea
Sværi, Bård Kjetil Bratli	Leading research technician		Technical support
Syrtveit, Astrid	Stud.Med.		Wik
Sæle, Anna Kristine Myrmel	PhD candidate	MD	Wik/Akslen
Sørlie, Therese	Adjunct professor	MD, PhD	CCBIO
Tandaric, Luka	PhD candidate	MS	Bjørge/McCormack
Tegnander, Amalie Fagerli	Stud.Med. (Medical Student Research Program)		Akslen/Wik
Thiery, Jean Paul	Adjunct professor	MD, PhD	CCBIO
Thomsen, Liv Cecilie Vestrheim	Researcher	MD, PhD	Gjertsen/Bjørge
Thurfjell, Viktoria	PhD candidate	MD	Strell
Tislevoll, Benedicte Sjo	PhD candidate	MD	Gjertsen
Torkildsen, Cecilie Fredvik	PhD candidate	MD	Bjørge
Tornaas, Stian	PhD candidate	MS	Costea
Tranvåg, Eirik Joakim	Guest Researcher	MD, PhD	Norheim
Trovik, Jone	Professor	MD, PhD	Krakstad
Tveiterås, Maria	PhD candidate	MS, MD	Reed
Van den Berg, Madeleine	Visiting student		Krakstad
Vethe, Heidrun	Postdoc	PhD	Akslen
Vidhammer, Eli Synnøve	Senior executive officer		Administration
Vikse, Hans Martin	Research technician		Technical support
Wagner-Larsen, Kari Strøno	PhD candidate	MD	Krakstad
Watnick, Randolph	Adjunct researcher	MD, PhD	CCBIO
Wik, Elisabeth	Associate professor	MD, PhD	Akslen/Wik
Winge, Ingeborg	Senior engineer	PhD	Akslen
Wogsland, Cara Ellen	Senior researcher	PhD	McCormack
Xenaki, Victoria	PhD candidate	DDS	Costea
Zaraq, Tariq Jan	Master student		Costea
Zeltz, Cedric	Researcher	PhD	Gullberg
Östman, Arne	Adjunct professor	MD, PhD	CCBIO
Øyan, Anne Margrethe	Senior scientist	MS, PhD	Kalland
Åse, Hildegunn Siv	PhD candidate	MD	Krakstad

CCBIO Annual Symposium

May 10-11 2022

CCBIO Investigators and Invited Speakers

Upper row, left to right: *Karl-Henning Kalland, Line Bjørge, Matthias Nees, Bjørn Tore Gjertsen, Malin Sund, Hani Gabra, Bob Langer, Roger Strand, Yamila T. Cleuren, Geir Olav Løken, Rolf K. Reed, Jean-Christophe Bourdon, Yves Aubert, Olli Kallioniemi.*

Middle rows, left to right: *Carina Strell, Srinivas Malladi, Marta Bertolaso, Anne Blanchard, Therese Sørlie, Daniel Öhlund, Ingeborg Winge, Sébastien Wälchli, Elisabeth Wik, Mark LaBarge, Bjørn Hofmann.*

Front row, left to right: *Oddbjørn Straume, John Cairns, Ian Mills, Christine Desmedt, Gooitzen van Dam, Rolf Brekken, Lars A. Akslen, Daniela Elena Costea, Donald Gullberg, Jim Lorens, Dominique Chu.*

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